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VIRAL HEPATITIS*

A Consideration of Certain Aspects of Current Importance to the Practicing Physician

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PHILADELPHIA

DURING recent years, the importance of viral hepatitis as a public-health and military problem has become increasingly apparent. The term "viral hepatitis" is used to include as a group the forms of hepatitis caused by filterable infectious agents that apparently are primarily hepatotropic and produce, as their outstanding clinical manifestations, evidences of liver injury that may or may not be associated with phenomena suggesting an infectious origin.

Viral hepatitis thus includes the two types of disease commonly referred to as infectious (epidemic) and homologous serum hepatitis. The available evidence indicates that at least two filterable agents, which tentatively can be classified as viruses, are concerned.[1-5] One, referred to below as virus IH, has been identified primarily with the clinical and epidemiologic syndrome of infectious (epidemic) hepatitis, which usually has an incubation period of fifteen to forty days. It perhaps has not been generally recognized that this virus may also be responsible for so-called "homologous serum hepatitis" occurring fifteen to forty days after "parenteral exposure" to a source of the virus through one of the mechanisms discussed below. More familiar is the classic syndrome of homologous serum hepatitis, the most distinctive feature of which is the long interval of two to four and a half months that elapses between "parenteral exposure" and the onset of the overt disease. The other of the two viruses mentioned above, and subsequently referred to as virus SH, appears to be mainly responsible for this syndrome. Homologous serum hepatitis thus should not be regarded as a single etiologic entity.

Evidence for the existence of at least these two hepatitis viruses (IH and SH types) has been described in detail elsewhere.[1-5] Further discussion here does not seem warranted except to call attention to the fact that the differences that have been demonstrated between these two types of hepatitis virus stand strongly on the mutually confirmatory experimental results obtained by three independent groups of investigators[1-5] and are supported by a large body of epidemiologic evidence.[1, 6, 7] Efforts to account for the various syndromes of viral hepatitis on the basis of a single virus fail to explain the consistent short incubation period following parenteral injection of IH viruses, the failure of SH viruses to induce overt disease when administered orally, and the lack of resistance (cross immunity) to infection by one virus in the presence of resistance (homologous immunity) to reinfection by the other.

At the present time, however, the problems presented by the two recognized types of viral hepatitis overlap, and, as no clinically applicable method for their specific differentiation has been developed, it is practical and useful to consider them together under the group term "viral hepatitis."

PUBLIC-HEALTH ASPECTS

Considered in the above sense, viral hepatitis is a widespread disease of high sporadic and epidemic incidence. The actual incidence must be considerably higher than the apparent incidence since the disease unfortunately is not universally reportable and because many cases, particularly those in which jaundice does not become overt, are unrecognized. The recognized cases alone, however, are sufficiently frequent to warrant recognition of viral hepatitis as an existing and potential public-health problem of major importance.

SPECIAL PROBLEMS IN DIAGNOSIS AND MANAGEMENT

Of considerable interest and clinical significance is the fact that viral hepatitis is being recognized with increasing frequency as an important cause of jaundice in the older age groups. Most of the infections in these patients appear to be of the virus

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SH type, and the increased incidence probably results in part from the greater frequency with which older persons are being exposed to the mechanisms whereby blood transmission of virus may occur. Possible explanations for the apparent predominance of virus SH types of infection in the older age groups have been discussed elsewhere.[1] Suffice it to say here that viral hepatitis not only is the most frequent cause of jaundice in children and young adults but also must now be regarded as a frequent cause of jaundice in older persons. This is of considerable clinical significance because the onset, particularly of the SH type, frequently is relatively silent and the course initially may resemble that of the familiar clinical picture of malignant or mechanical obstruction of the extrahepatic biliary tract, with progressively increasing jaundice and, occasionally, clay-colored stools. Phenomena suggesting an infectious origin are frequently absent. Recognition and accurate differential diagnosis are of extreme importance, since surgical exploration of the patient with acute hepatitis is associated with a high mortality. It is essential, therefore, that viral hepatitis be considered as a possibility in every jaundiced patient regardless of age.

Aside from the difficulties viral hepatitis presents in differential diagnosis, the disease, even when recognized, constitutes a further problem in management and disposition. This results from the fact that the duration of disability and incapacitation in the favorable uncomplicated overt case averages approximately six weeks. Even under the best of conditions a small percentage of patients suffer disability for longer periods as a result of the tendency of the disease to relapse, and, in a still smaller percentage, to become chronic. Although the overall mortality is low, estimated in large outbreaks as approximately 0.2 per cent, it has been as high as 20 per cent in certain small outbreaks.[1] Viral hepatitis, therefore, is never to be regarded lightly, and the initial course of the disease frequently provides no clinical warnings of an impending relapse or fatal outcome. These tendencies to natural relapse and chronicity, or fatal termination, may be exaggerated by delayed recognition and improper management. Early recognition and treatment are therefore of considerable importance. In addition, it is during the first and second weeks of jaundice that the intelligent use of a group of hepatic tests provides the most reliable and helpful assistance in differential diagnosis. All too frequently the performance of such studies early in the disease is deferred in the hope that the jaundice will subside or the cause will become obvious with the passage of time and that the patient thereby will be saved the expense and trouble of laboratory studies. The importance of obtaining a "baseline" group of hepatic tests in every jaundiced patient within the first two weeks of jaundice cannot be overemphasized. With few exceptions, clinical phenomena cannot be depended upon for differential diagnosis, and the proper decision between medical and surgical treatment is at times life saving. For this reason, every jaundiced patient deserves prompt laboratory investigation regardless of how typical the clinical phenomena appear. As the maximum diagnostic assistance from laboratory investigations is obtained soon after jaundice is detected, failure to take advantage of such assistance at that time may be regretted later. It is not implied that laboratory tests alone will differentiate "medical" and "surgical" jaundice. Properly selected and interpreted tests applied at the right time, however, will substantially increase the incidence of correct differentiation of those two conditions or, at least, will assist in the decision concerning immediate, if not ultimate, management.

Newer Aspects of Etiology and Epidemiology

The increasing medicolegal importance of viral hepatitis deserves special comment. Unfortunately, the available information indicates that a considerable, as yet unestimable, proportion of the cases of viral hepatitis are consequences of certain indispensable technics of medical practice. This is of great immediate concern to all, for it not only threatens the continued use of some of the most important and irreplaceable therapeutic weapons, blood and plasma, but also potentially involves certain costly, protracted and difficult changes in medical technic, which, ignored or not recognized, may occasionally lead to suits for malpractice.

An example is an incident, recently described in the foreign-correspondence section of the *Journal of the American Medical Association*,[8] that resulted in the imprisonment of a physician in Italy. The justifications for the action taken in this case cannot be evaluated from the data presented, but the episode serves as a warning of the potential dangers involved.

Time does not permit a detailed discussion of this problem. It is possible only to point out, in a general way, some of the matters involved. Figure 1 represents an attempt to portray diagrammatically a tentative working concept of the etiology and epidemiology of viral hepatitis. Some of the general factors concerned in the transmission of hepatitis are as follows: blood and feces are the only proved sources of hepatitis virus, which is apparently present in high concentration, since extremely small quantities may be infectious; the viruses survive for long periods under variable conditions and resist many procedures that eliminate or inactivate most infectious agents, including desiccation, extremes of temperature, filtration, commonly used plasma preservatives (such as merthiolate) and chlorination of water under certain conditions; the virus may be present in blood or feces without previous, associated or subsequent symptoms or signs.

No extrahuman host has as yet been recognized. Therefore, discussion must at present start and end with the human host (Fig. 1). Hepatitis viruses IH and SH may both be acquired from human blood. Only the former has been shown to be present in the feces. Neither has been proved conclusively to be present, or absent, in urine and nasopharyngeal secretions, but present information suggests that these are not potent sources of hepatitis virus, at least during the active stages of the disease. Transmission of hepatitis virus IH from feces through one or more of the mechanisms shown in Figure 1 probably accounts for a large proportion of the naturally acquired infections, both sporadic and epidemic. At the present time, there is little that one can do to interrupt this chain of events other than apply the usual sanitary measures indicated for control of all intestinal pathogens.

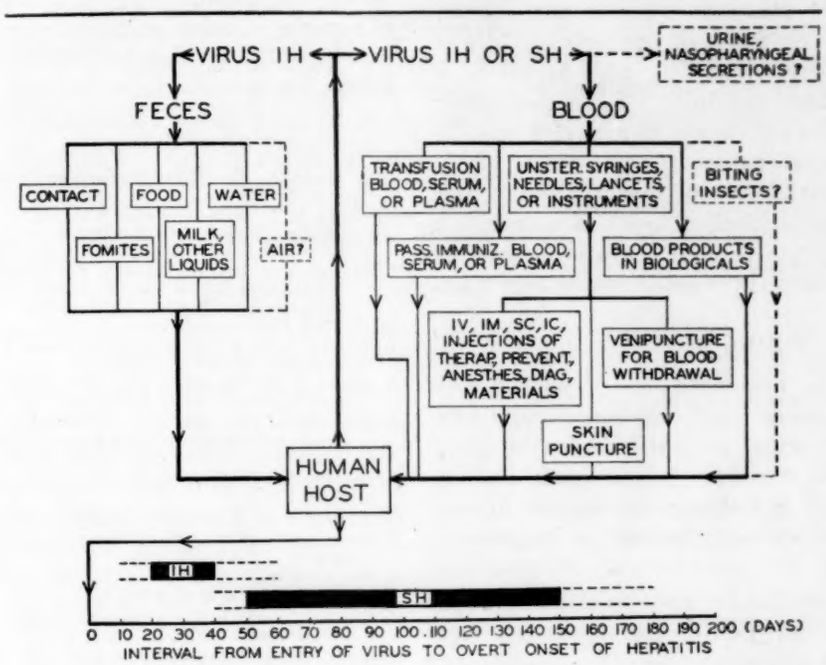
VIRUS IH
VIRUS IH OR SH
URINE, NASOPHARYNGEAL SECRETIONS ?
FECES
BLOOD
CONTACT
FOOD
WATER
FOMITES
MILK, OTHER LIQUIDS
AIR?
TRANSFUSION BLOOD, SERUM, OR PLASMA
UNSTER. SYRINGES, NEEDLES, LANCETS, OR INSTRUMENTS
BITING INSECTS?
PASS. IMMUNIZ. BLOOD, SERUM, OR PLASMA
BLOOD PRODUCTS IN BIOLOGICALS
IV, IM, SC, IC, INJECTIONS OF THERAP, PREVENT, ANESTHES, DIAG, MATERIALS
VENIPUNCTURE FOR BLOOD WITHDRAWAL
SKIN PUNCTURE
HUMAN HOST
IH
SH
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200 (DAYS)
INTERVAL FROM ENTRY OF VIRUS TO OVERT ONSET OF HEPATITIS

FIGURE 1. *Concept of the Etiology and Epidemiology of Viral Hepatitis.*

The mechanisms of transfer of hepatitis virus through blood and its derivatives are of particular interest. The special factors involved in the prevention of blood transmission include the fact that minute quantities (0.01 cc. or less) are infective; all methods developed to date that are capable of inactivating the virus in blood or plasma render these materials unsatisfactory or unsafe for human use; there is as yet no practical method for detecting the virus in blood or plasma, and no method for detecting infected donors; as pointed out above, the viruses may appear in the blood without previous, associated or subsequent symptoms or signs; it is not known whether the virus persists or recurs in the blood after recovery from acute hepatitis; development of a method for inactivating the virus in whole blood or plasma will solve only part of the problem; the virus in human serum albumin solutions is apparently inactivated by present methods of processing (heating at 60°C. for ten hours). In Figure 1, the recognized mechanisms through which the hepatitis virus may be acquired from blood are enclosed in solid lines. Three of these — namely, the use of human blood, plasma or serum for transfusion, passive immunization and as a component of biologicals — are well established links in the epidemiologic chain.[1] Transmission through these mechanisms is not yet completely preventable, but the frequency can be decreased by recognition and adherence, so far as possible, to the following principles: transfusion of the blood, plasma or serum should be avoided whenever possible and used only when the indication is greater than the risk (the choices in order of increasing risk are human serum albumin, whole blood, single plasma units, cross-matching beings required, small plasma pools and large plasma pools); donors should be excluded if they have been exposed to a potential source of the virus during the preceding six months, if they have had unexplained or positive symptoms during the previous six months or if icterus, hepatomegaly and positive laboratory findings are present at the time of bleeding; the recipient's record should contain data identifying the product received; and the blood-bank record should

identify the recipients and donors. Furthermore, failure to recognize and weigh the potential risk may have important medicolegal implications.

A fourth mechanism, although difficult to prove directly, is supported by a large body of epidemiologic evidence.[9-22] It must therefore be recognized that the hepatitis virus may be transmitted by means of improperly sterilized syringes, needles, lancets and other instruments that have been in contact with human blood (Fig. 1). As such transmission is preventable, all practical precautions must be taken. Although it is difficult and perhaps impossible to prove infection of individual cases by this mechanism, failure to recognize the potentialities is again of medicolegal importance and formed the basis of the case against the Italian physician cited above. Some of the possible means by which the hepatitis virus may gain access to a person through the medium of inadequately sterilized instruments are shown in Figure 1 as subheadings under this mechanism.

Finally, the potential role of insect bites in the transmission of these viruses in blood is mentioned (broken lines, Fig. 1), although there is as yet no direct evidence of natural transmission in this way.

Summary

Viral hepatitis is presented as a widespread disease of high sporadic and epidemic incidence caused by at least two, primarily hepatotropic, filterable, infectious agents whose outstanding clinical manifestation is evidence of hepatic injury with or without associated phenomena suggesting an infectious origin.

The fact that viral hepatitis involves all age groups is emphasized, and its apparently increasing frequency as a cause of jaundice in the older age groups is discussed, particularly in relation to the importance of its consideration in every jaundiced patient regardless of age and the clinical phenomena.

The public-health, military, and individual significance of the disease is stressed, with special reference to morbidity, mortality and its unfortunate relation to certain indispensable medical technics.

The increasing medicolegal importance of the disease to the practicing physician is emphasized. This new aspect has developed with the recent recognition of the potential relation between viral hepatitis and certain medical technics. This relation is illustrated by reference to a diagram summarizing the available knowledge concerning the sources of the hepatitis viruses and the mechanisms by which they are transferred from person to person. The responsibility of the physician in the interruption of certain of these potential mechanisms is indicated.

References

1. Neefe, J. R. Recent advances in knowledge of "virus hepatitis." *M. Clin. North America* **39**:1407-1443, 1946.
2. Havens, W. P., Jr. Epidemiological studies on infectious hepatitis. *Am. J. Pub. Health* **36**:37-44, 1946.
3. Paul, J. R., Havens, W. P., Jr., Sabin, A. B., and Philip, C. B. Transmission experiments in serum jaundice and infectious hepatitis. *J. A. M. A.* **128**:911-915, 1945.
4. Neefe, J. R., Gellis, S. S., and Stokes, J., Jr. Homologous serum hepatitis and infectious (epidemic) hepatitis: studies in volunteers bearing on immunological and other characteristics of etiological agents. *Am. J. Med.* **1**:3-22, 1946.
5. McCallum, F. O., Havens, W. P., Jr., and Neefe, J. R. Papers in *Proceedings of the Fourth International Congresses on Tropical Medicine and Malaria, May 10 to 18, 1948* (in press).
6. Gauld, R. L. Epidemiological field studies on infectious hepatitis in Mediterranean Theater of Operations: relation between vaccine jaundice and infectious hepatitis. *Am. J. Hyg.* **43**:310, 1946.
7. McFarlan, A. M., and Chesney, G. Hepatitis following injection of mumps convalescent plasma: reports from American Red Cross-Harvard Field Hospital Unit: epidemiology of hepatitis. *Lancet* **1**:816, 1944.
8. Foreign Letters. Epidemic of homologous serum hepatitis. *J. A. M.A.* **137**:209, 1948.
9. Bigger, J. W. Jaundice in syphilitics under treatment: possible transmission of virus. *Lancet* **1**:457, 1943.
10. Salaman, M. H., King, A. J., Williams, D. I., and Nicol, C. S. Prevention of jaundice resulting from antisyphilitic treatment. *Lancet* **2**:7, 1944.
11. Sheehan, H. J. Epidemiology of infective hepatitis. *Lancet* **2**:8-11, 1944.
12. Hartfall, S. J. Jaundice in rheumatoid arthritis. *Lancet* **2**:358, 1944.
13. Beattie, J., and Marshall, J. Aetiology of postarsphenamine jaundice. *Brit. M. J.* **1**:547-550, 1944.
14. Loutit, J. F., and Maunsell, K. Prevention of homologous serum jaundice. *Brit. M. J.* **2**:759, 1945.
15. Droller, H. Outbreak of hepatitis in diabetic clinic. *Brit. M. J.* **1**: 623-625, 1945.
16. Darmady, E. M., and Harwick, C. Syringe-transmitted hepatitis. *Lancet* **2**:106,1945.
17. Memorandum by Medical Officers of Ministry of Health: role of syringes in transmission of jaundice. *Lancet* **2**:116-119, 1945.
18. Editorial. Syringes, serum, and jaundice. *Brit. M. J.* **1**:810, 1945.
19. Editorial. Syringe transmitted hepatitis. *J. A. M. A.* **129**:278, 1945.
20. Mendelssohn, K., and Witts, L. J. Transmission of infection during withdrawal of blood. *Brit. M. J.* **1**:625, 1945.
21. Howells, L., and Kerr, J. D. O. Hepatitis after penicillin injections. *Lancet* **1**:51, 1946.
22. Capps, R. B., Sborov, V., and Scheiffley, C. S. Syringe-transmitted epidemic of infectious hepatitis: with observations regarding incidence and nature of infected donors. *J. A. M. A.* **136**:819-824, 1948.

A SURVEY OF RECENT THERAPEUTIC MEASURES IN CIRRHOSIS OF THE LIVER*

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ELEVEN years have elapsed since Patek[1] first reported the effectiveness of a nutritious diet in the treatment of cirrhosis of the liver. On the basis of the rapidly accumulating evidence that cirrhosis can be produced in animals on a low-protein diet and prevented by the addition of certain food factors,[2-5] a nutritious diet accompanied by abstinence, when there is a history of alcohol addiction, is now the accepted method of treatment. In this communication consideration is given to certain practical aspects of the dietary treatment of cirrhosis, particularly the quantity of fat allowed, the place of vitamin and specific amino acid supplements and the importance of a low-sodium diet in the control of ascites and edema. In addition a critique is presented of the more recent method of treatment of patients with esophageal varices and ascites who are not improved by dietary means alone.

The recently reported experiences of Patek's group[6-8] in the dietary treatment of cirrhosis are summarized in Table 1. It should be pointed out that the controls were taken from hospital admissions between the years 1920 and 1940, when other important therapeutic measures such as chemotherapy and blood transfusions were not as generally available as they have been in the last ten years. The results are nevertheless impressive and have been confirmed,[9-11] and in spite of the absence of a better controlled series the importance of a nutritious diet in the treatment regime seems well established.

The mere prescription of such a diet is not sufficient. A patient with cirrhosis may have severe anorexia and must be tempted with an attractive menu. He may have to be fed by attendants or maintained by tube or parenteral feeding until his appetite returns. That there is still room for improvement in the treatment of cirrhosis even under the ideal conditions of a research service is shown by the fact that only 61 of 124 cases treated by Patek's group showed clinical improvement fulfilling the following three criteria: gain in weight and strength; disappearance of ascites, edema and jaundice; and changes toward normal values of the liver-function tests.[8]

A number of observers believe that fat should be restricted in the diet provided to patients with liver disease. This conception probably has arisen from the evidence that a high-fat intake hastens the appearance of cirrhosis in animals on a low-protein diet, and secondly that patients with biliary-tract obstruction generally have a fatty-food intolerance. In experimental animals, however, an adequate protein diet protects the liver from the injurious effects of fat. Moreover, patients with cirrhosis rarely have a fatty-food intolerance. Indeed, Patek's[8] patients were given 175 gm. of fat a day, together with 365 gm. of carbohydrate and 140 gm. of protein. This amount of fat is necessary to ensure palatability of the diet, and no ill effects were noted by Patek in his patients. Restricting the fat content to 50 gm. a day, as advocated by some,[10, 11] results in an unpalatable, low-calorie diet that discourages the patient from taking the one "medicine" really important for him — food. Thus, no restriction of fat in the diet of patients with cirrhosis seems indicated unless obesity makes a restriction in calories necessary.

TABLE 1. *Duration of Life in Cirrhosis of the Liver after the Onset of Ascites in 124 Treated Patients and 230 Control Cases.**

PERIOD OF SURVIVAL	TREATED CASES	CONTROL CASES
yr.	%	%
One	65	39
Two	50	21
Five	30	7

*Based on studies reported by Patek et al.[6-8]

The history of prolonged poor food intake, together with signs suggestive of vitamin deficiency present in some cirrhotic patients, has made the addition of vitamin supplements to most treatment regimes common. However, some doubt has been cast on the need for the administration of large quantities of purified vitamins. It is generally agreed that the liver is a storehouse for both the water-soluble and fat-soluble vitamins and that these stores are reduced in a cirrhotic liver. But the signs thought to be due to vitamin deficiency often do not respond as well to vigorous treatment as they do in patients without liver disease. It has been suggested[12] that in some patients with cirrhosis there exists an intrinsic, rather than extrinsic, deficiency — that is, a diminished ability of the liver to utilize the vitamins supplied to it (for example, as coenzymes). In addition, it is theoretically pos-

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sible that niacin in large doses may be harmful to patients with fatty livers. Since a portion of administered niacin is excreted as the methyl derivative, the vitamin has been given to animals to hasten the development of cirrhosis on a deficient diet by reducing the effectiveness of choline and methionine.[13] Gillman and Gillman[14] found that pellagrous children with fatty livers became worse when given large quantities of vitamins, whereas

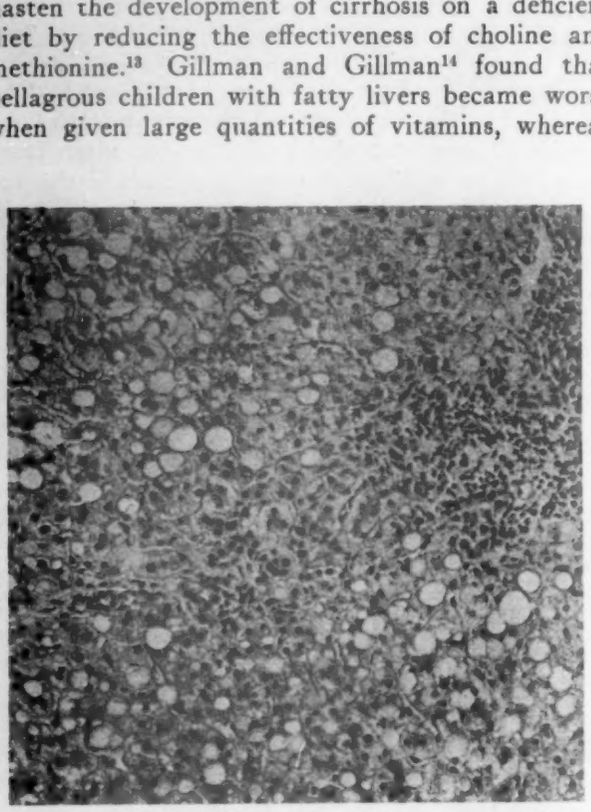

FIGURE 1. *Punch Biopsy of the Liver of a Chronic Alcoholic Patient Who Entered the Hospital Deeply Jaundiced and Close to Delirium Tremens.*
There is moderate fatty metamorphosis and cellular infiltration.

the fat rapidly disappeared from their livers on treatment with dried hog's stomach. They suggested that the poor results of massive vitamin therapy might be due to an antilipotropic effect of niacin. Since, therefore, large doses of the purified vitamins do not appear necessary and may be harmful, it seems wise to administer them only in the usual therapeutic quantities, or better to rely on the nutritious diet and, if necessary, crude food supplements may be given in addition.

Three nutrients that have been shown to be important in the prevention and treatment of experimental dietary liver injury in animals are choline, a source of methyl groups, and the sulfur-containing amino acids, methionine and cystine. Methionine is also an important source of methyl groups for the synthesis of choline. The exact modes of action of these substances and the possible existence of others are the subjects of present research. However, since methionine and choline have already been used rather extensively in the clinical treatment of liver disease, it is important to determine whether or not they are useful.

In a disease as chronic and at the same time as variable in its course as cirrhosis it is extremely difficult to assess the efficacy of a single therapeutic measure. Adequate controls are necessary, and yet many of the reports of the clinical use of methionine and choline in cirrhosis are uncontrolled[15-17] In four recent studies with controls[10, 11, 18, 19] the groups given choline or methionine showed an apparent decrease in mortality rate and somewhat greater and faster improvement than those treated with a nutritious diet alone, but the size of each group was too small to be significant and the method of selecting cases not always clear. Larger numbers of patients, strictly alternated, control and treated, are necessary to eliminate effects resulting from the many uncontrolled variables encountered in such a study. Finally, a nutritious diet furnishes in itself relatively large amounts of choline and methionine. Until the science of nutrition has become exact enough to indicate all the nutrients necessary in health and disease and the precise quantities required, it seems better to supply those nutrients as food rather than purified chemicals.

If the physician cannot induce the patient to eat a nutritious diet, crude food complements such

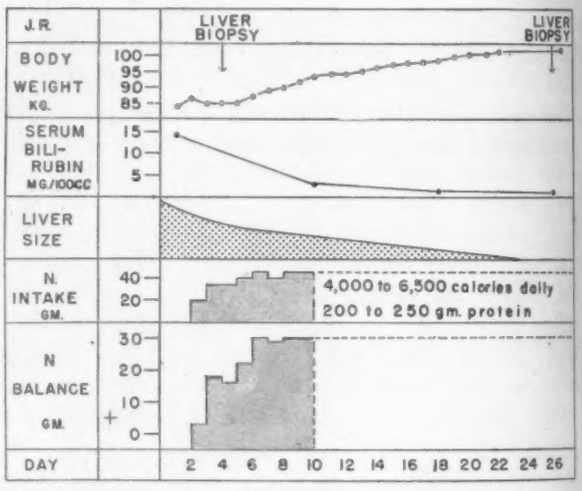

FIGURE 2. *Clinical Course of the Patient Whose Biopsies Are Shown in Figure 1 and 3.*

as brewer's yeast powder, high-protein milk drinks and liver products by mouth, intramuscularly or intravenously, may be employed. Labby and his associates[20] reported excellent results, primarily in the form of appetite stimulation, with frequently administered intravenous crude liver extract, but here again simultaneous controls were lacking and their patients were in general of a higher economic and social stratum than the usual charity-hospital population, and thus were more amenable to all forms of therapy.

The dramatic improvement that may take place in patients with liver disease who eat well is illustrated by the course of a thirty-five-year-old longshoreman who entered the Boston City Hospital deeply jaundiced and close to delirium tremens after a prolonged drinking bout during which he ate almost nothing. A punch biopsy taken before treatment (Fig. 1) shows the fatty metamorphosis characteristic of the liver cells in such patients and, in addition, a quite marked cellular infiltration around the portal areas. Figure 2 summarizes the patient's clinical course. His appetite was excellent, food intake (without supplements) was enormous, and he retained a considerable proportion of the nitrogen administered. He gained 15 kg. (33 pounds), and his serum bilirubin and liver size rapidly receded to normal. Figure 3 shows his liver three weeks after therapy was begun, essentially normal. Thus early changes in the liver may be completely reversible if the patient stops drinking and eats well. This patient could hardly have improved more rapidly had choline and methionine been added to his diet.

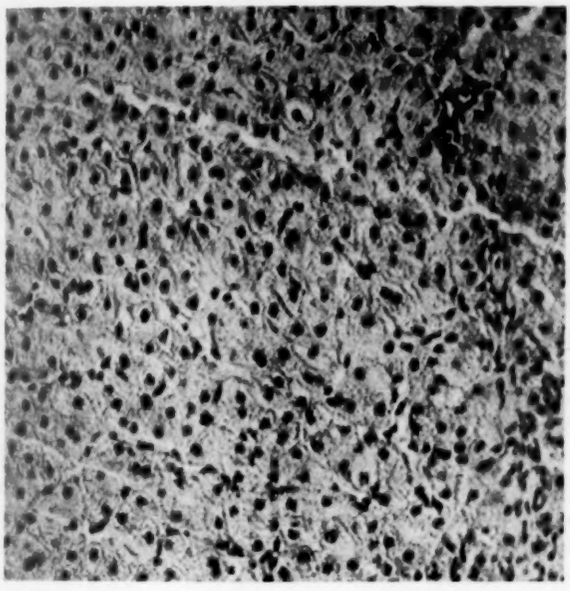

FIGURE 3. *Punch Biopsy of the Liver Obtained Three Weeks after the One Illustrated in Figure 1.*

The fat has completely disappeared, and the biopsy is essentially normal.

The rapid recovery to be expected in early cirrhosis as contrasted with the later forms of the disease has been observed by several investigators.[21, 22] Indeed, it is becoming increasingly apparent that many alcoholic patients with early cirrhosis may live out their normal life span if they abstain from alcohol while continuing to eat a nutritious diet. This fact emphasizes the need for finding early cases by the freer use of sensitive liver-function tests and punch biopsy as part of any attempt to reduce the mortality from the disease. In fact, all of 24 patients entering the Boston City Hospital with delirium tremens but without significant clinical signs of cirrhosis were found by punch biopsy to have abnormal amounts of fat in their livers and 14 to have early, asymptomatic fibrosis.[23] Gratifying results can be obtained in this group of patients, so large in any charity hospital, if intensive treatment is instituted by the combined efforts of internist, psychiatrist and social worker.

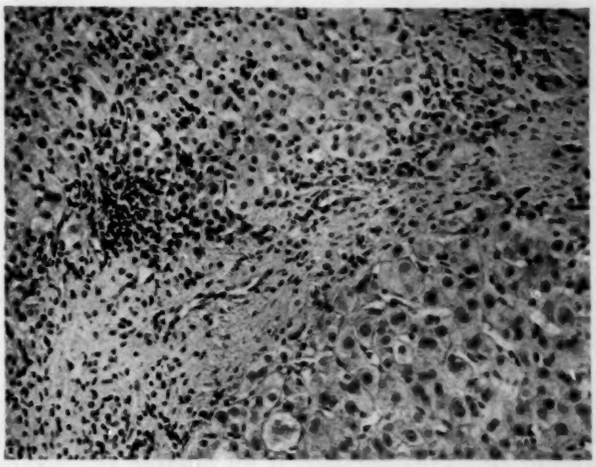

FIGURE 4. *Punch Biopsy of the Liver of a Chronic Alcoholic Patient with Massive Ascites Who Had Been Treated for Three Months with a Highly Nutritious Diet.*

Fairly normal-appearing liver cells are encased in thick bands of fibrous tissues.

In the treatment of the more chronic forms of liver disease other problems are encountered, especially recurrent ascites. Figure 4 is a photomicrograph of a biopsy of the liver of a chronic alcoholic patient who entered the hospital with massive ascites and who for three months before biopsy required frequent paracenteses although he was treated vigorously with a nutritious diet and almost daily intravenous liver extract. The biopsy section reveals fairly normal liver cells encased in thick bands of fibrous tissue. This is the kind of stabilized patient referred to as having intractable ascites — the kind who feels and eats well but requires frequent paracenteses and who, although he may occasionally be freed of ascites, may die at any time of bleeding from ruptured esophageal varices.

How much dietary treatment can do for the patient with cirrhosis who is relatively asymptomatic except for episodes of hematemesis has not been established. It is doubtful whether diet can alter the fibrous tissue that obstructs the hepatic circulation and shifts large amounts of blood from the liver into the collaterals. Reports of such sur-

gical procedures as injection of the esophageal collateral veins,[24, 25] mediastinotomy[26] and gastrectomy[27] and the various operations for shunting blood from the portal to the systemic circulation[28-30] are appearing in increasing numbers. Positive criteria indicating the procedure of choice are not yet available. Many more operations and controlled studies are necessary.

The results of A. H. Blakemore,[31] who has had a large experience in the shunting operations, are illustrated in Table 2. He has tried one of several shunting procedures on 43 patients with cirrhosis with a decreasing operative mortality and an increasing number of the anastomoses remaining patent. But the operation is formidable and should probably be undertaken only in patients in the best of condition. Again, this large series is still too small and the patients not followed long enough for final conclusions to be drawn.

TABLE 2. *Results of Blood-Shunting Operations for the Relief of Ascites and Bleeding Varices in Cirrhosis of the Liver.**

Purpose of Operation	No. of Cases	Postoperative Deaths	Patients Surviving 1 Year or More without Recurrence	Total Deaths over 3 Years	Recurrence of Bleeding (Mild)	Disappearance of Ascites
Ascites	6	2	2	—	—	—
Hemorrhage†	37	7 (19%)	12 (32%)	14 (38%)	2	3

*Based on personal communication from A. H. Blakemore, of New York City.
†Three patients also had ascites.

Two years ago Crosby and Cooney[32] described what appeared to be an ideal surgical method for the relief of intractable ascites. A modified Murphy button was inserted into the abdominal wall connecting the peritoneal cavity with the subcutaneous tissues, resulting in a constant emptying of ascitic fluid into the subcutaneous space whence it was returned to the circulation. The series was small, but the results were good. In contrast, the results of this procedure performed on 14 service patients from the Boston City Hospital and the Mount Auburn Hospital, Cambridge, have been poor.[33] Five patients died in the postoperative period, 6 in from three weeks to one year and 2 in from one to two years after the operation; 1 is surviving three years after operation. Of the 9 who survived the postoperative period, 4 had a recurrence of ascites within one month, 3 within three months, and 1 within fourteen months. No functioning buttons were found in the 9 autopsied patients: 4 were plugged with fibrin, and 3 with omentum, and in 5 a pseudoperitoneal cavity similar to that recently described in detail by Welch[34] had formed. Only 4 of the 14 patients were definitely improved for appreciable lengths of time.

It should be pointed out that this series of patients, under service rather than private care, is not directly comparable with those of others who have achieved good results with this operation. Optimal nutritional therapy was not usually possible after the patients left the hospital, and some of the operations were done in a rush of enthusiasm before the patients had been adequately prepared. However, patients who are abstemious and well treated by diet frequently have spontaneous remissions. The poor end results and high postoperative mortality of the patients in this series of "button" operations raise grave doubts of its value. It may be that the modification recently described by Lord[35] will prolong the period of relief from ascites. No other reports of this procedure have appeared.

Recently, two significant developments have been added to the medical treatment of intractable ascites: the intravenous administration of concentrated human serum albumin, and the provision of diets low in salt. Janeway and his associates[36] and Thorn et al.[37] observed that albumin injections in doses large enough to raise the serum albumin concentration to normal induced little more than a transient diuresis. Patek and his coworkers[38] confirmed this in a short-term experiment. But Kunkel et al.[39] reported the complete disappearance of ascites in 14 of 15 patients given albumin intravenously. As might be expected, those with early ascites and generalized edema responded more readily than patients with long-standing ascites and other evidences of excessive portal obstruction.

In an effort to elucidate the reasons for these discrepancies and the mechanisms responsible for the formation and disappearance of ascites in cirrhosis, Faloon and his associates[40] studied 29 patients with ascites treated with intravenous albumin, some over long periods. Four patients had a diuresis that began soon after the first albumin administration, 7 had a delayed response, and 3 responded only after the salt content of the diet had been reduced. There were 6 failures — 6 patients who did not respond although their serum albumin concentration was maintained at between 3 and 4 gm. per 100 cc. for long periods. The results in 9 patients were classified as indeterminate because the pa-

tients were neither treated nor followed long enough.*

Responses just as erratic as those after albumin administration have been seen in patients treated with diet alone and in those given mercurial diuretics. In an effort to find a common metabolic defect altered in patients showing a response to these several measures, sodium-balance studies were performed by Faloon et al.[41] The patients with decompensated cirrhosis were found to be unable to excrete administered sodium except in very small amounts. When diuresis occurred, but with 6 gm. of sodium chloride given in addition. He remained in positive sodium and water balance, gained 12 pounds in weight and required an average of 20 gm. of albumin a day to maintain a normal serum albumin concentration. On withdrawal of the added 6 gm. of salt his sodium balance became negative, and he stopped gaining weight and required daily only 11 gm. of albumin to maintain the same serum albumin concentration.

The mechanism of this inability to excrete sodium is obscure, but the therapeutic implications are obvious. The frequency of abdominal paracentesis

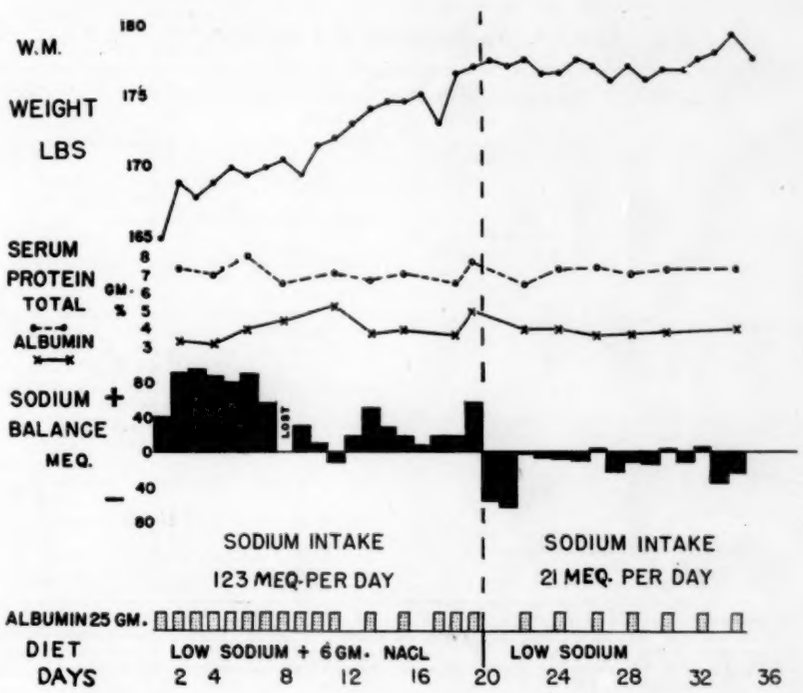

FIGURE 5. *The Effect of Sodium Restriction in the Diet of a Patient Who Is Accumulating Ascites.*

The serum albumin level had previously been raised to normal by intravenous concentrated salt-poor human albumin. This was continued at a rate necessary to maintain the serum albumin at a normal level.

whether spontaneous or accompanying albumin or mercurial administration, urinary sodium rose markedly and a negative sodium balance ensued.

Figure 5 illustrates the effect of withholding salt from the diet of a patient who had required frequent paracenteses in spite of a serum protein concentration maintained at normal by the intravenous administration of albumin. Over a twenty-day period he was provided with a low-sodium diet, containing about 1.25 gm. of sodium chloride a day, can be reduced if the patient is maintained on a low-sodium diet supplemented, if desired, by ammonium chloride and mercurial diuretics. Concentrated human albumin is an expensive and in some cases perhaps a somewhat dangerous adjunct to this regime. The best results of albumin administration are seen in patients with massive edema and ascites who have not required paracentesis. The importance of restricting salt is best illustrated by the following calculations. Extrarenal loss of sodium chloride under moderate temperature conditions has been found to remain fairly constant, at about 1 gm. a day.[42, 43] Urinary loss in a cirrhotic patient who is accumulating ascites is rarely more than 0.5 gm. a day, regardless of intake. If the sodium chloride intake is limited to less than 1.5 gm. a day, little fluid will be retained. When the

*Adverse reactions that may have been associated with albumin administration were encountered in 10 patients, a third of the series reported by Faloon et al.[40] Directly related to the albumin injections were 2 cases of acute pulmonary edema, 1 fatal, 1 of chill and fever followed by coma and death, 1 of fatal nosebleed, and a fatal esophageal hemorrhage. One patient bled on two occasions from a gastric ulcer soon after albumin injections. Two other patients bled from ruptured esophageal varices four and seven days after albumin therapy had been stopped; both died. Two patients developed pleural effusions. It was difficult to ascertain how directly the albumin therapy contributed to these deaths. However, it is apparent that such therapy may not be without danger and should be used with caution.

intake is 6 gm., as in the ordinary hospital diet without added salt, around 500 cc. may be retained. When the intake is 10 gm., as in the usual American diet salted to taste, approximately a liter of fluid, equal to 2 pounds of body weight, may be retained a day.

Patients with ascites have not generally been treated with a low-salt diet in the past because it is difficult to prepare a nutritious diet, particularly one adequate in protein, which is at the same time low in salt. The diet employed by Faloon et al., presented in Table 3, contains only approximately 0.8 gm. of sodium chloride, but there are 131 gm. of protein, 309 gm. of carbohydrate and 143 gm. of fat — approximately 3000 calories. The salt content is kept low by the use of bread of low-salt content, sweet butter, vegetables cooked or canned without added salt and a low-sodium milk powder, or other low-sodium protein supplement. The taste of the diet may be improved by the employment of a salt substitute — one in which the sodium, not the chloride ion, is replaced. No untoward symptoms due to sodium or chloride deprivation were noted in this study, which was performed in the winter months, but such symptoms might develop during the hot summer months in patients being maintained free of ascites on a low-salt diet.

Finally, the importance of bed rest in the treatment of chronic hepatic disease should be mentioned. There is general agreement that it is one of the most important therapeutic measures, as pointed out by Jones and Volwiler[44] in their review of the treatment of chronic hepatitis. This clinical observation is supported by the experimental work of Bradley[45] on the relation of posture to hepatic blood flow.

TABLE 3. *Nutritious Diet Low in Sodium.**

FOOD	AMOUNT	HOUSEHOLD MEASURES	CARBOHYDRATE	PROTEIN	FAT	SODIUM
	gm.		*gm.*	*gm.*	*gm.*	*mg.*
Breakfast:						
Orange	100	1 (medium)	11.2	0.9	0.2	0.2
Shredded wheat	30	1 biscuit	23.6	3.1	0.4	0.6
Bread	50	2 slices	25.0	4.0	2.0	1.0
Butter	20	2 pats	—	0.2	16.2	1.0
Egg	50	1 egg	0.4	6.4	5.8	70.0
Cream (light)	100	3 ounces	4.0	2.9	20.0	52.0
Sugar	25	2 tablespoonfuls	25.0	—	—	—
Low-sodium milk	150	4 glasses per day	57.0	40.5	42.0	15.0
Dinner:						
Beef	100	3 ⅓ ounces	—	23.1	7.6	53.0
Potato	100	½ cup	19.1	2.0	0.1	0.6
Carrots	100	⅓ cup	9.3	1.2	0.3	31.0
Beans	100	½ cup	7.7	2.4	0.2	0.8
Bread	50	2 slices	25.0	4.0	2.0	1.0
Butter	20	2 pats	—	0.2	16.2	1.0
Bananas	150	1 (large)	34.5	1.8	0.3	0.2
Supper:						
Chicken	100	½ breast	—	26.2	10.4	94.0
Peas	100	½ cup	17.7	6.7	0.4	0.9
Tomatoes	100	1 (medium)	4.0	1.0	0.3	3.0
Bread	50	2 slices	25.0	4.0	2.0	1.0
Butter	20	2 pats	—	0.2	16.2	1.0
Peaches (canned)	100	2 halves	18.2	0.4	0.1	6.0
Totals			306.7	131.2	142.7	333.3

*This diet, which was compiled by Miss Kathleen A. Clinton, dietitian at the Thorndike Memorial Laboratory, contains approximately 3000 calories and 330 mg. of sodium or 835 mg. of sodium chloride. Caloric values were calculated from standard food tables. Sodium values were taken from *Sodium and Potassium Analyses of Foods and Waters* (fifth list), Mead Johnson and Company, Evansville, Indiana, and *The Chemical Composition of Foods* (second edition), by R. A. McCance and E. M. Widdowson (Brooklyn: Chemical Publishing Co., 1947).

Fresh fruits and vegetables should be used. Butter must be sweet or washed. Bread must be salt-poor and may be obtained at some bakeries or made at home with salt-poor flour and low-sodium milk powder instead of whole milk. Cottage cheese is the only cheese allowed but should be washed. Processed, canned or smoked meats should not be used. Low-sodium milk powder (Lonalac) may be obtained from Mead Johnson & Company. Cereals allowed: Farina, plain, Wheatena, Instant Ralston, Maltex, Oatmeal (rolled oats), Puffed Rice, Puffed Wheat, and Shredded Wheat. Many quick-cooking cereals and dry cereals are high in salt.

SUMMARY

The employment of a palatable, nutritious diet adequate in protein and not reduced in fat content has, with chemotherapy and blood transfusions, improved the prognosis of hepatic cirrhosis.

Such nutrients as vitamins, methionine and choline are probably supplied in adequate amounts by the nutritious diet described. If food cannot be taken in a sufficient quantity, crude food complements should be administered.

The role of surgery in the treatment of portal hypertension is still not established, but it seems probable that the mortality from ruptured esophageal varices may be reduced by procedures such as portal-systemic venous anastomosis.

Intractable ascites is best treated by a nutritious diet, low in salt, supplemented by mercurial and other diuretics and, if necessary, by intravenously administered, salt-poor, concentrated serum albumin.

References

1. Patek, A. J., Jr. Treatment of alcoholic cirrhosis of liver with high vitamin therapy. *Proc. Soc. Exper. Biol. & Med.* **37**:329, 1937.
2. György, P., and Goldblatt, H. Observations on conditions of dietary hepatic injury (necrosis, cirrhosis) in rats. *J. Exper. Med.* **75**:355-368, 1942.
3. Rich, A. R., and Hamilton, J. D. Experimental production of cirrhosis of liver by means of deficient diet. *Bull. Johns Hopkins Hosp.* **66**:185-198, 1940.
4. Lillie, R. D., Ashburn, L. L., Sebrell, W. H., Daft, F. S., and Lowry, J. U. Histogenesis and repair of hepatic cirrhosis in rats produced on low protein diets and preventable with choline. *Pub. Health Rep.* **57**:502-508, 1942.
5. Himsworth, H. P., and Glynn, L. E. Massive hepatic necrosis and diffuse hepatic fibrosis (acute yellow atrophy and portal cirrhosis): their production by means of diet. *Clin. Sc.* **5**:93-123, 1944.
6. Patek, A. J., Jr., and Post, J. Treatment of cirrhosis of liver by nutritious diet and supplements rich in vitamin B complex. *J. Clin. Investigation* **20**:481-505, 1941.
7. Patek, A. J., Jr. Evaluation of dietary factors in treatment of Laennec's cirrhosis of liver. *J. Mt. Sinai Hosp.* **14**:1-7, 1947.
8. Patek, A. J., Jr., Post, J., Ratnoff, O. D., Mankin, H., and Hillman, R. W. Dietary treatment of cirrhosis of liver: results in one hundred and twenty-four patients observed during a ten-year period. *J. A. M. A.* **138**:543-549, 1948.
9. Kimball, S., and Chapple, W. A. C. Laennec's cirrhosis: effect of therapy in increasing life expectancy. *Gastroenterology* **8**:185-190, 1947.
10. Morrison, L. M. New methods of therapy in cirrhosis of liver. *J. A. M. A.* **134**:673-676, 1947.
11. Steigmann, F. Efficacy of lipotropic substances in treatment of cirrhosis of liver. *J. A. M. A.* **137**:239-243, 1948.
12. Hoagland, C. L. Therapy of liver disease. *Bull. New York Acad. Med.* **21**:537-556, 1945.
13. Handler, P., and Dubin, I. N. Significance of fatty infiltration in development of hepatic cirrhosis due to choline deficiency. *J. Nutrition* **31**:141-159, 1946.
14. Gillman, T., and Gillman, J. Powdered stomach in treatment of fatty liver and other manifestations of infantile pellagra: its significance with reference to problems of edema and steatorrhea in infants and adults. *Arch. Int. Med.* **76**:63-74, 1945.
15. Russakoff, A. H., and Blumberg, H. Choline as adjuvant to dietary therapy of cirrhosis of liver. *Ann. Int. Med.* **21**:848-862, 1944.
16. Broun, G. O., and Muether, R. O. Treatment of hepatic cirrhosis with choline chloride and diet low in fat and cholesterol. *J. A. M. A.* **118**:1403, 1942.
17. Barker, W. H. Modern treatment of cirrhosis of liver. *M. Clin. North America* **29**:273-293, 1945.
18. Beams, A. J. Treatment of cirrhosis of liver with choline and cystine. *J. A. M. A.* **130**:190-194, 1946.
19. Beams, A. J., and Endicott, E. T. Histologic changes in livers of patients with cirrhosis treated with methionine. *Gastroenterology* **9**: 718-735, 1947.
20. Labby, D. H., Shank, R. E., Kunkel, H. G., and Hoagland, C. L. Intravenous therapy of cirrhosis of liver. *J. A. M. A.* **133**:1181-1190, 1947.
21. Patek, A. J., Jr. Dietary treatment of Laennec's cirrhosis with special reference to early stages of disease. *Bull. New York Acad. Med.* **19**: 498-506, 1943.
22. Lewis, J. H., Taylor, F. H. L., and Davidson, C. S. Protein nutrition: therapeutic use of digest of liver protein, especially in patients with cirrhosis of liver. *New Eng. J. Med.* **236**:351-359, 1947.
23. Chalmers, T. C., Murphy, T. L., and Taft, E. B. Incidence, character and course of liver disease in chronic alcoholics as determined by needle biopsy. *J. Clin. Investigation* **27**:528, 1948.
24. Moersch, H. J. Treatment of esophageal varices by injection of sclerosing solution. *J. A. M. A.* **135**:754-757, 1947.
25. Patterson, C. O., and Rouse, M. O. Injection treatment of esophageal varices. *J. A. M. A.* **130**:384-386, 1946.
26. Som, M. L., and Garlock, J. H. New approach to treatment of esophageal varices. *J. A. M. A.* **135**:628, 1947.
27. Wangensteen, O. H. Ulcer problem: etiology with special reference to interrelationship between vascular and acid-peptic digestive factors: characterization of satisfactory operation which will protect against recurrent ulcer. *Canad. M. A. J.* **53**:309-331, 1945.
28. Blakemore, A. H. Indications for portocaval anastomosis — analysis of cases. *Surg., Gynec. & Obst.* **84**:645-653, 1947.
29. Linton, R. R. Portocaval shunts in treatment of portal hypertension: with special reference to patients previously operated upon. *New Eng. J. Med.* **238**:723-727, 1948.
30. Blalock, A. Use of shunt or by-pass operations in treatment of certain circulatory disorders, including portal hypertension and pulmonic stenosis. *Ann. Surg.* **125**:129-141, 1947.
31. Blakemore, A. H. Personal communication.
32. Crosby, R. C., and Cooney, E. A. Surgical treatment of ascites. *New Eng. J. Med.* **235**:581-585, 1946.
33. Chalmers, T. C., Eckhardt, R. D., and Davidson, C. S. Unpublished data.
34. Welch, K. J. Failure of peritoneal-button operation for ascites: report of two cases. *New Eng. J. Med.* **237**:735-737, 1947.
35. Lord, J. W., Jr. Modification of Crosby–Cooney operation for intractable ascites due to cirrhosis of liver. *J. A. M. A.* **136**:767, 1948.
36. Janeway, C. A., et al. Chemical, clinical and immunological studies on products of human plasma fractionation. VII. Concentrated human serum albumin: albumin in treatment of shock: safety of albumin: albumin in treatment of hypoproteinemia. *J. Clin. Investigation* **23**:465-490, 1944.
37. Thorn, G. W., Armstrong, S. H., and Davenport, V. D. Chemical, clinical and immunological studies on products of human plasma fractionation. XXXI. Use of salt-poor concentrated human serum albumin solution in treatment of hepatic cirrhosis. *J. Clin. Investigation* **25**:304-323, 1946.
38. Patek, A. J., Jr., Mankin, H., Colcher, H., Lowell, A., and Earle, D. P., Jr. Effects of intravenous injection of concentrated human serum albumin upon blood plasma, ascites and renal functions in three patients with cirrhosis of liver. *J. Clin. Investigation* **27**: 135-145, 1948.
39. Kunkel, H. G., Labby, D. H., Ahrens, E. L., Shank, R. E., and Hoagland, C. L. Use of concentrated human serum albumin in treatment of cirrhosis of liver. *J. Clin. Investigation* **27**:305-319, 1948.
40. Faloon, W. W., Eckhardt, R. D., Murphy, T. L., Cooper, A. M., and Davidson, C. S. Evaluation of human serum albumin in treatment of cirrhosis of liver. *J. Clin. Investigation* (in press).
41. Faloon, W. W., Eckhardt, R. D., Cooper, A. M., and Davidson, C. S. Effect of human serum albumin, mercurial diuretics, and low sodium diet on sodium excretion in patients with cirrhosis of liver. *J. Clin. Investigation* (in press).
42. Freyberg, R. H., and Grant, R. L. Loss of minerals through skin of normal humans when sweating is avoided. *J. Clin. Investigation* **16**:729-731, 1937.
43. Mackay, E. M., and Butler, A. M. Studies of sodium and potassium metabolism. Effect of potassium on water and sodium balances in normal subjects and patients with Bright's disease. *J. Clin. Investigation* **14**:923-939, 1935.
44. Jones, C. M., and Volwiler, W. Therapeutic considerations in subacute and chronic hepatitis. *M. Clin. North America* **31**:1059-1077, 1947.
45. Bradley, S. M. Variations in hepatic blood flow in man during health and disease. *New Eng. J. Med.* **240**:456-461, 1949.

VARIATIONS IN HEPATIC BLOOD FLOW IN MAN DURING HEALTH AND DISEASE*

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THE liver acts as a selective barrier between the gastrointestinal tract and the systemic circulation, metabolizing, detoxifying and elaborating for further physiologic disposition various substances that enter the portal blood during digestion. Unquestionably, the rich and complex vasculature of the liver serves these processes by providing an adequate supply of oxygen and raw materials. In addition, this extensive vascularity itself may indicate an important role in cardiovascular dynamics.

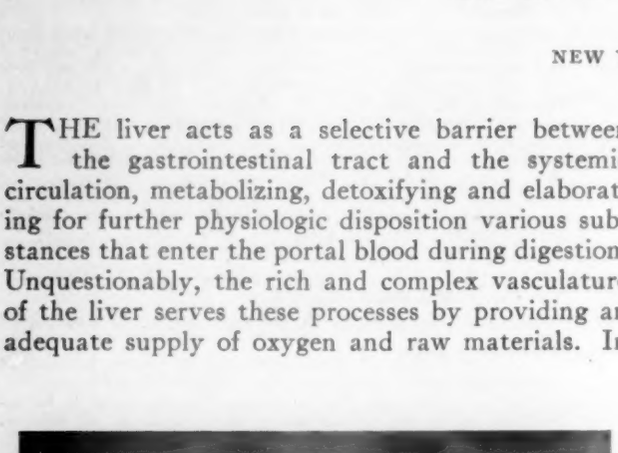

FIGURE 1. *Catheterization of the Hepatic Veins.*
In this skiagraph, the radio-opaque catheter may be seen passing through the right axillary and subclavian veins to the superior vena cava and thence through the right atrium and upper portion of the inferior vena cava to a vein in the right lobe of the liver.

Unfortunately, very little is known about the physiology of the hepatic circulation, largely because it is so inaccessible. Traumatic surgical manipulations required for its study are obviously inapplicable in the study of man and are open to serious question when used in the study of animals. Gross distortions of function arising from operative injury and anesthesia complicate the interpretation of data obtained under these circumstances and prevent quantitative evaluation of discrete parenchymal activities.

The recent development of methods for the atraumatic catheterization of the great veins by Cournand and his co-workers[1] at Bellevue Hospital has provided a means by which hepatic venous blood may be sampled at frequent intervals in human subjects without difficulty. By this method a long, radio-opaque ureteral catheter may be inserted into an antecubital vein, and passed under fluoroscopic control through the superior vena cava and right atrium into the inferior vena cava and thence into one of the right hepatic veins (Fig. 1). Blood may then be withdrawn through the catheter as desired. A vast new field of study has thus been opened to exploration. The hepatic extraction of various substances may be measured directly, and hepatic blood flow may be estimated by a clearance technic.[2] Bromsulfalein (BSP) has been used for the latter purpose since it is removed from the blood almost exclusively by the liver.[3] Hence it seems reasonable to assume that the rate of intravenous infusion of BSP is equal to the rate of hepatic BSP removal when the BSP concentration in the blood is kept constant. Dividing the calculated rate of removal by the difference between BSP concentrations in hepatic venous and peripheral arterial (or venous) blood will yield a value approximating hepatic blood flow. The principle of this procedure is familiar as the basis of the methods by which cardiac output and renal blood flow are measured. Since the dye may be removed to a certain extent by tissues outside the liver, since the concentration in peripheral arterial blood may not equal the concentration in the portal vein, and since the blood coming from only one hepatic vein is sampled and may not therefore be representative of the liver as a whole, the figure for hepatic blood flow has been referred to as "*estimated* hepatic blood flow" (EHBF). However, values given by this method are in agreement with those obtained by other procedures[4] not open to these particular errors and may be considered valid measures of the hepatic circulation. It is evident, however, that EHBF is a measure of volume of blood flowing into the splanchnic vasculature each minute, without reference to the relative contributions of the mesenteric, splenic, gastric and hepatic arterial inflows.

In 50 normal resting human subjects studied at the Evans Memorial Hospital in Boston, EHBF ranged from 950 to 1840 cc. per minute per 1.73 M² of body surface, averaging 1490 cc. per minute.

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Thus, approximately 25 per cent of the basal cardiac output appears to pass through the splanchnic circuit. The kidneys and the brain also receive large amounts of blood, approximately 1200 cc. passing through the kidneys[5] and 800 cc. through the brain,[6] on the average, each minute. Since the cerebral circulation must be kept constant within relatively narrow limits it is obvious that the major task of vascular regulation must fall upon the liver and kidneys. Numerous studies[7-10] have demonstrated conclusively that the renal blood flow is highly variable and quickly adjusted to current requirements in such a manner as to maintain arterial pressure and to compensate for relatively inadequate responses of cardiac output as in chronic anemia or orthostasis. Indeed, this activity may be carried to such an extreme that irreversible renal damage may occur after prolonged intrarenal vasoconstriction during shock. Studies of the hepatic circulation indicate that the liver also plays a prominent role in vascular homeostasis.

In animal experiments, a remarkable variation in hepatic blood flow has been observed, ranging in one study[11] from 40 to 160 cc. per minute per 100 gm. of liver tissue. The variability has been attributed to irregularity of blood flow through the sinusoids. Direct observation of the transilluminated liver has revealed free flow of blood through only about a quarter of the sinusoids at any moment, owing to intermittent passage through individual vessels.[12] With hyperemia, a larger number of sinusoids open to permit passage of a correspondingly larger volume of blood, whereas during hepatic ischemia intermittency becomes more marked. In human subjects the range of blood flow was relatively large, but it was by no means of this magnitude and appeared indeed chiefly a function of the errors inherent in the method of measurement. Moreover, the values for BSP extraction by different parts of the liver agreed fairly closely. Hence it appears that blood is distributed evenly throughout the liver and that changes in blood flow may be attributed to diffuse rather than to gross focal alterations in vasomotor activity. Of course, it is impossible to say whether vasomotor activity responsible for changes in EHBF also affects the splanchnic arterioles, but it seems wholly likely that it does, since vasoconstriction in the liver alone would operate to impound blood in the portal area with detrimental effect upon systemic hemodynamics. Exclusively hepatic vasodilation would produce the same effect by raising the pressure in the hepatic arterial capillaries, with a resulting dynamic obstruction to portal venous outflow.

A study of hepatic circulatory dynamics during exercise was undertaken in collaboration with Dr. E. DeF. Baldwin at the Columbia–Presbyterian Medical Center for the purpose of assessing integration of the hepatic circulation into the total circulatory system during stress. Simultaneous measurements of cardiac output (by the direct Fick method), renal blood flow (by the sodium p-amino hippurate clearance) and hepatic blood flow (by BSP clearance) were made in normal volunteers prior to and during exercise, which consisted of bicycling against weights in the recumbent position. The findings during such a study are presented in Figure 2. Blood-pressure recordings, measured in another person under similar circumstances, have been inserted in Figure 2 to provide a complete picture of hemodynamic events. Although little change in blood pressure occurred during exercise the output of the heart almost doubled. At the same time the blood flow through the kidney and the liver (that is, the splanchnic vascular bed) fell sharply, the hepatic blood flow to a much greater extent than the renal. The blood flow to other circuits — the brain, heart and especially the muscles — thus increased to a greater extent than is indicated by the change in cardiac output. In this way blood was made available at the expense of the liver and kidneys, while the heart was spared

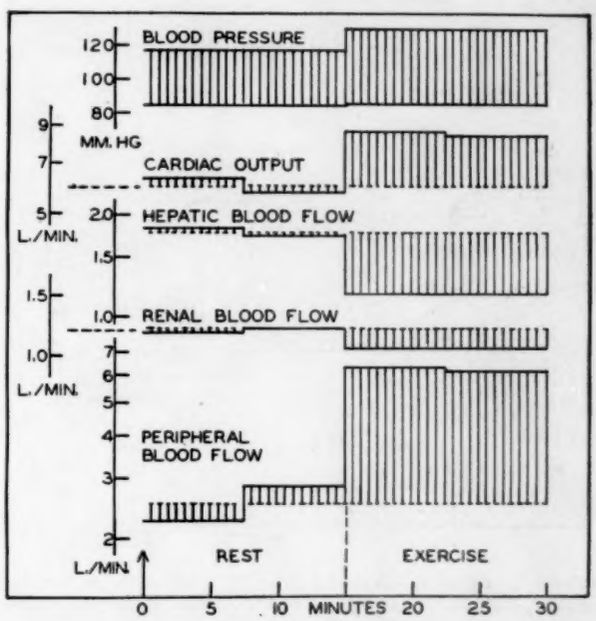

FIGURE 2. *Effect of Exercise on Estimated Hepatic Blood Flow, Renal Blood Flow, Peripheral Blood Flow and Arterial Pressure in Man.*

With the exception of the arterial pressure, which was measured sphygmomanometrically in a separate study, all determinations were made as nearly simultaneously as possible under standard conditions. The sum of the values for estimated hepatic blood flow (bromsulfalein method) and effective renal blood flow (sodium p-aminohippurate clearance corrected for the hematocrit) was subtracted from the cardiac output (direct Fick method) to obtain a figure for peripheral blood flow. Exercise (bicycling against weights in recumbency) was started thirty minutes after the beginning of the study. Cardiac output increased, but blood flow through the renal and hepatoportal circuits fell, thus permitting a considerably larger increment in blood flow to the periphery than would have been possible on the basis of the change in cardiac output alone.

the effort required to expel sufficient blood to meet the total need imposed by exercising muscle.

The subjects of this investigation were placed under the stress of exercise alone as far as it was possible. Hence they were maintained in the recumbent position throughout. The upright position imposes an independent burden upon the circulation and if coupled with exercise might be expected to influence the picture and make interpretation difficult. It seemed of great interest to know whether standing alters the hepatic circulation as much as it affects the total circulation, and so a study of the question was undertaken at the Evans Memorial Hospital in Boston.[13] These workers have investigated the question very thoroughly, and there is little reason to doubt the accuracy of the synthesis presented here. In Figure 3, arterial pressure measured with the Hamilton membrane manometer and hepatic blood flow determined before and after assumption of the upright position (with the use of a tilt-table) are compared with figures for cardiac output (obtained by Dr. André Cournand) and renal blood flow (taken from figures published by H. W. Smith[7]) determined in other normal subjects under similar conditions. It is evident that the hepatic and renal hemodynamic adjustments were similar to those observed in response to exercise, whereas cardiac output was reduced by gravitational interference with the return of blood to the heart. Hence, the hepatic and splanchnic vasoconstriction implicit in the reduction of blood flow in spite of an elevated mean arterial pressure operate to maintain blood flow to areas more sensitive to the effects of ischemia.

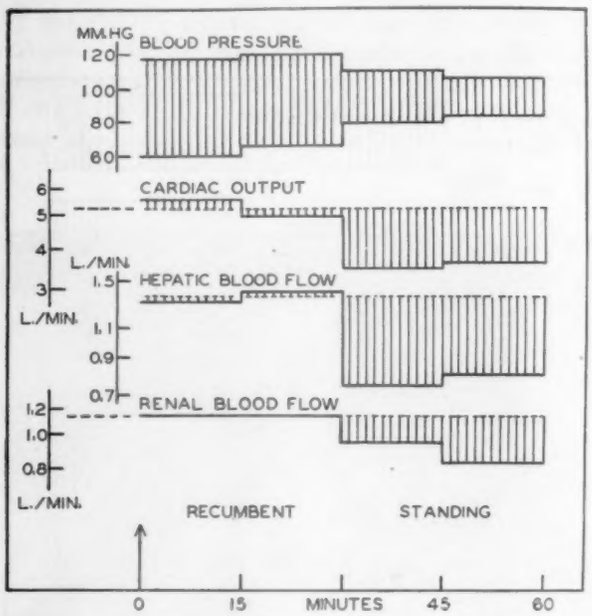

FIGURE 3. *Effect of Standing Upright upon Arterial Pressure, Cardiac Output, Estimated Hepatic Blood Flow and Renal Blood Flow in Man.*

This composite picture of the vascular readjustments after a change in position from recumbency to standing by means of a tilt-table is based upon figures for arterial pressure (Hamilton manometer) and estimated hepatic blood flow determined simultaneously in one patient and for cardiac output (provided through the courtesy of Dr. André Cournand) and renal blood flow (Chasis et al.[7]) obtained in other patients under similar conditions. Since cardiac output was not measured at the same time as renal and hepatic blood flow, the peripheral blood flow could not be calculated. With the postural change there was a fall in cardiac output without much change in mean arterial pressure although the pulse pressure decreased, apparently as a result of diminished stroke volume. Vasoconstriction in the hepatoportal and renal vascular beds apparently contributes to the increased total peripheral vascular resistance implicit in this phenomenon, thus accounting for the reduction in local flows despite maintenance of arterial pressure.

What bearing may these findings have upon understanding of disease of the liver? Obviously, any attempt to answer this question enters the realm of speculation. The only conclusions we are entitled to draw from these observations relate exclusively to normal man and throw light only upon normal regulatory mechanisms. Nonetheless, the temptation is irresistible, and with this warning it is perhaps permissible to make certain tentative inferences. There is growing agreement that convalescence from inflammatory hepatic disease and, in particular, from infectious hepatitis is disturbed by early mobilization and return to activity.[14, 15] Since an adequate supply of blood is usually essential in hastening and maintaining the repair of damaged tissue, and since ordinary activity involves exertion in the upright position, it is possible that the vasoconstriction demonstrable in these studies is one of the factors involved in causing relapse and retarding recovery.

Another factor that comes to mind in such speculations is the possible influence of minor febrile infections. Fever has been shown[16] to produce a striking physiologic disturbance that affects nearly every organ system in the body. The response of the cardiovascular system during pyrogenic reactions is particularly striking, and it is not surprising therefore to find that the hepatic vasculature participates actively in these readjustments.

A composite picture of the typical circulatory events observed during the pyrogenic reaction in 2 normal subjects is presented in Figure 4. Hepatic blood flow was determined in 1, and cardiac output, arterial pressure and renal blood flow in the other. The marked increase in vascular activity is clearly evident. Cardiac output increased after the chill phase in association with increased blood flow through both kidney and liver. The increment in cardiac output appears to be accounted for in large part by the augmentation in renal and hepatic blood flow. Of considerable interest is the appearance of hepatocellular dysfunction, which was evident in the marked depression of the extraction of BSP from the blood perfusing the liver. Bromsulfalein was no longer efficiently eliminated from the blood by the liver, and retention of BSP was

demonstrable for a period of at least twenty-four hours after the onset of the reaction. It is not so well known, perhaps, that pyrogen may have such an effect even when fever does not develop. In a clinical investigation of this factor[17] typhoid vaccine was administered to patients undergoing fever therapy, after premedication with aminopyrine. As a result, the body temperature remained unchanged, but the physiologic response was otherwise unaltered. In 2 of 8 subjects, slight tender enlargement of the liver was demonstrable, there was an increase in serum alkaline phosphatase, and the cephalin-cholesterol flocculation test became positive, reverting to normal in a few days. In these subjects the detrimental effect of the pyrogenic

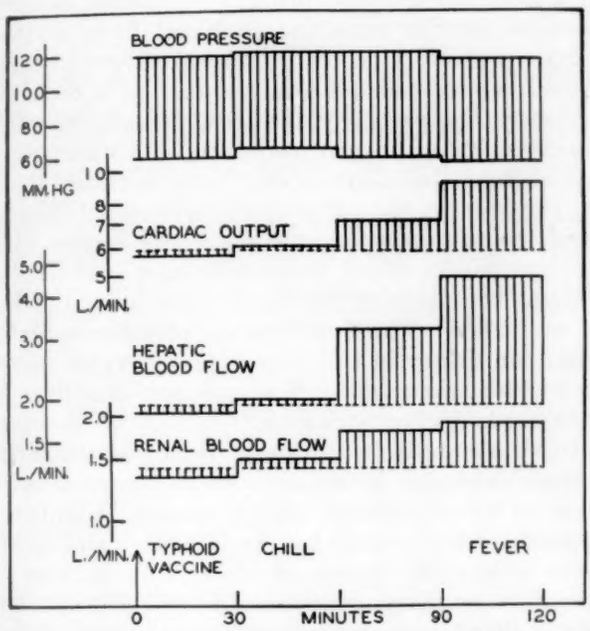

FIGURE 4. *Effect of the Pyrogenic Reaction upon Arterial Pressure, Cardiac Output, Estimated Hepatic Blood Flow and Renal Blood Flow in Man.*

Results from two studies, one in which hepatic blood flow was determined after intravenous administration of typhoid vaccine (100,000,000 organisms) and a second in which arterial pressure, cardiac output (ballistocardiograph) and renal blood flow were measured after a dose of pyrogenic inulin (100 mg. intravenously) are combined in this graph. For the sake of convenience the pyrogen is noted here only as "typhoid vaccine." During pyrexia, hepatic hyperemia develops in association with renal hyperemia as the cardiac output increases.

substance was evident despite the absence of fever. It is a very short step indeed to the inference that similar reactions with or without fever would be undesirable — perhaps even disastrous — during convalescence from inflammatory hepatic disease.

Disturbances of hepatic blood flow may be expected to result from the structural disorganization following severe injury by toxic agents or infection. Cirrhosis, in particular, is associated with a striking deformation of the hepatic blood vessels. Beautiful plastic reconstructions have been made by the introduction of an injection mass of celloidin, neoprene or other materials under pressure into the hepatic artery and portal veins, permitting it to harden and then carefully digesting away the parenchymal tissue, as demonstrated by McIndoe.[18] These models show in a most convincing and graphic manner how Laennec's cirrhosis affects the blood

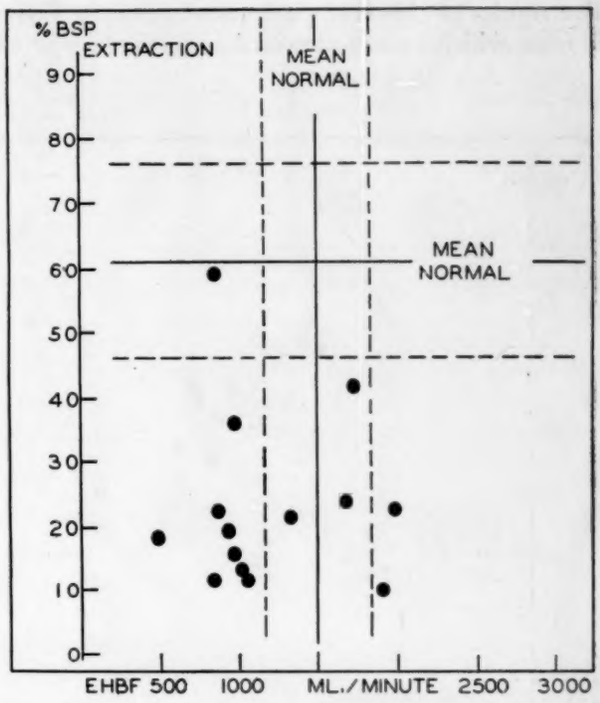

FIGURE 5. *Estimated Hepatic Blood Flow (EHBF) and Bromsulfalein (BSP) Excretion in Cirrhosis of the Liver.*

vessels of the liver. One can see at a glance the simplification, reduction and distortion of both arterial and portal venous radicles, in sharp contrast to the complex and massive arrangement of the innumerable interwoven vessels of the normal. On anatomic grounds alone one would almost certainly say that hepatic blood flow is reduced. Nonetheless, in the absence of supporting functional evidence, the question has remained open since vasodilation or shunting, even in such a circulatory bed as this, might result in hyperemia. Indeed, evidence has been brought forward in support of the claim that the hepatic outflow may be augmented, rather than reduced, perhaps chiefly as a result of enhanced arterial inflow, which may impose a dynamic resistance to portal venous inflow and contribute to the elevation of portal pressure. Thus, in 1907 Herrick[19] found that the hepatic artery may be perfused with saline solution in the liver removed after death, more easily in the cirrhotic than in the normal person. And Dock,[20] more recently, has found decreased arterial resistance to

perfusion with kerosene in alcoholic cirrhosis, but not in other types of the disorder. Obviously, such post-mortem changes may have no bearing on events during life. Hence, in collaboration with Dr. F. J. Ingelfinger, in Boston, and Drs. A. E. Groff and G. P. Bradley, in New York, hepatic blood flow was estimated in a group of patients with well established Laennec's cirrhosis and chronic alcoholism, and in 3 persons with cirrhosis due to periportal fibrosis, schistosomiasis and syphilis, respectively.[21] The results of this study are summarized in Figure 5, from which values obtained in patients who excreted less than 10 per cent of BSP have been excluded. In only 4 subjects did the value for blood flow exceed the normal mean value of EHBF.

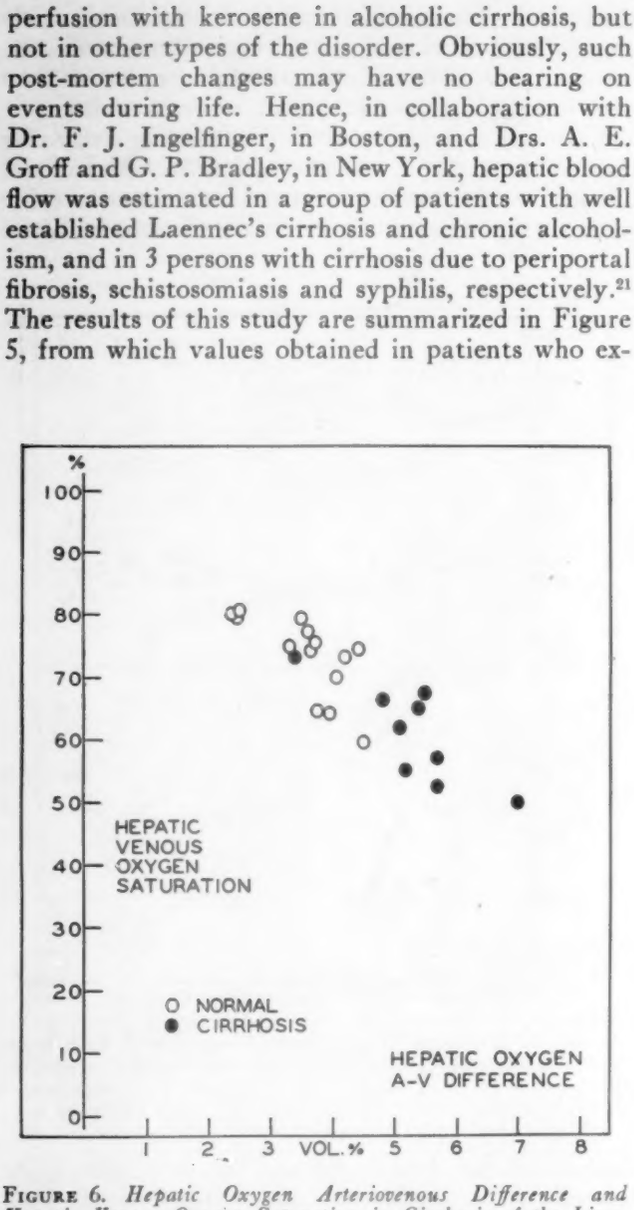

FIGURE 6. *Hepatic Oxygen Arteriovenous Difference and Hepatic Venous Oxygen Saturation in Cirrhosis of the Liver. With one exception the values for hepatic oxygen arteriovenous difference were depressed in cirrhosis (closed circles) below the normal values (open circles). There was an associated but less striking reduction in hepatic venous oxygen saturation.*

In 9, EHBF fell below the lowest normal figure. It should be noted that the values for hepatic blood flow are subject to error as result of the marked depression in the ability of the liver to remove BSP in all but 1 member of this series. Such an error would result in falsely high values for EHBF since the removal of BSP by extrahepatic tissues would contribute disproportionately to the total calculated removal rate. Hence the low values actually observed are the more significant of a true reduction in blood flow. The reduction in BSP excretion is particularly interesting. It may indicate arteriovenous shunting, perfusion of a large mass of non-extracting scar tissue or failure of damaged parenchymal cells to remove the dye from blood passing through the liver. Studies of hepatic oxygen excretion were made to assess the relative importance of these possibilities.

In Figure 6, the values for hepatic oxygen arteriovenous concentration differences are plotted against those for hepatic venous oxygen saturation in normal subjects and patients with cirrhosis. It may be seen that, with one exception, the hepatic oxygen arteriovenous difference in cirrhotic patients exceeded the normal range, and in most cases there was evidence of increased hepatic venous unsaturation. However, splanchnic oxygen consumption did not increase, for the increment in hepatic oxygen arteriovenous difference usually failed even to compensate for the reduction in blood flow, so that oxygen consumption tended to fall. These changes would be expected to follow a reduction in the mass of operative parenchymal tissue associated with maintenance of oxygen consumption per unit mass of residual tissue, at a relatively constant level. In the kidney, the oxygen arteriovenous difference tends to remain within narrow limits despite wide fluctuations in blood flow, indicating variation of oxygen consumption by renal tissue as a function of blood flow. The liver appears to differ radically from the kidney in this respect since oxygen excretion rises when blood flow through the liver is decreased during standing,[22, 23] and it therefore seems reasonable to ascribe increased hepatoportal oxygen excretion during cirrhosis to a more sluggish flow of blood through active tissues. Continued normal oxygen uptake by the intestines and spleen from a smaller volume of blood may account in part for the change in hepatic arteriovenous difference. But the portal arteriovenous oxygen difference is small (0.93 vol. per cent in each of 2 patients with cirrhosis and portal hypertension at operation), and the hepatic arteriovenous difference may be high in cirrhosis after ligation of the portal vein.[23] It may be inferred, therefore, that hepatic tissue is the most important site of oxygen uptake and that augmented oxygen excretion indicates relative ischemia of hepatic parenchyma. Hence, it appears on functional grounds that hepatic flow is greatly reduced in cirrhosis of the liver, regardless of etiology, as a result of an increased vascular resistance that acts to produce a relative ischemia of hepatic tissues, in which excretive — that is, parenchymal — cells figure much less prominently than in the normal organ. These observations are consistent with the view that fibrotic contraction impedes the flow of blood through the liver and that parenchymal injury thus has primacy in production of the structural changes of cirrhosis. Nonetheless, it is likely that the obstruction to blood flow may perpetuate and exaggerate the fundamental lesion.

There is little doubt that this obstruction is largely responsible for the elevation in the portal venous pressure, and for the sequelae of that portentous development.

In this discussion an attempt has been made to indicate an approach to the detailed analysis of hepatic function and dysfunction in man. On the basis of the studies described here and those of many other workers one can assign to the liver a role of importance not only in metabolic activities but also in cardiovascular dynamics, since it provides, with the kidney, a kind of hemodynamic buffer against undue stress. Although the implications of this concept are not yet completely explored, it is evident that the hepatoportal circulation has become a matter of more than passing interest to students of cardiovascular physiology and disease.

References

1. Cournand, A., and Ranges, H. A. Catheterization of right auricle in man. *Proc. Soc. Exper. Biol. & Med.* **46**:462-466, 1941.
2. Bradley, S. E., Ingelfinger, F. J., Bradley, G. P., and Curry, J. J. Estimation of hepatic blood flow in man. *J. Clin. Investigation* **24**:890-897, 1945.
3. Cantarow, A., Wirts, C. W., Snape, W. J., and Miller, L. L. Excretion of bilirubin and bromsulfalein in bile. *Am. J. Physiol.* **154**:211-219, 1948.
4. Myers, J. D. Hepatic blood flow and splanchnic oxygen consumption of man — their estimation from urea production or bromsulphalein excretion during catheterization of hepatic veins. *J. Clin. Investigation* **26**:1130-1137, 1947.
5. Smith, H. W. William Henry Welch Lectures. II. Application of saturation methods to study of glomerular and tubular function in human kidney. *J. Mt. Sinai Hosp.* **10**:59-108, 1943.
6. Kety, S. S., and Schmidt, C. F. Nitrous oxide method for quantitative determination of cerebral blood flow in man: theory, procedure and normal values. *J. Clin. Investigation* **27**:476-483, 1948.
7. Chasis, H., Ranges, H. A., Goldring, W., and Smith, H. W. Control of renal blood flow and glomerular filtration in normal man. *J. Clin. Investigation* **17**:683-697, 1938.
8. Smith, H. W. Physiology of renal circulation. *Harvey Lectures* **35**: 166-222, 1940.
9. Lauson, H. D., Bradley, S. E., and Cournand, A. Renal circulation in shock. *J. Clin. Investigation* **23**:381-402, 1944.
10. Bradley, S. E., and Bradley, G. P. Renal function during chronic anemia in man. *Blood* **2**:192-202, 1947.
11. Grindlay, J. H., Herrick, J. F., and Mann, F. C. Measurement of blood flow of liver. *Am. J. Physiol.* **132**:489-496, 1941.
12. Wakim, K. G., and Mann, F. C. Intrahepatic circulation of blood. *Anat. Rec.* **82**:233-253, 1942.
13. Culbertson, J. W., Wilkins, R. W., Ingelfinger, F. J., and Bradley, S. E. Effect of upright posture upon hepatic blood flow in normal and hypertensive human subjects. *J. Clin. Investigation* **26**:1178, 1947.
14. Barker, M. H., Capps, R. B., and Allen, F. W. Acute infectious hepatitis in Mediterranean theater, including acute hepatitis without jaundice. *J. A. M. A.* **128**:997-1003, 1945.
15. Hoagland, C. L. Therapy of liver diseases. *Bull. New York Acad. Med.* **21**:537-556, 1945.
16. Bradley, S. E., Chasis, H., Goldring, W., and Smith, H. W. Hemodynamic alterations in normotensive and hypertensive subjects during pyrogenic reaction. *J. Clin. Investigation* **24**:749-758, 1945.
17. Bradley, S. E., and Conan, N. J. Estimated hepatic blood flow and bromsulfalein extraction in normal man during pyrogenic reaction. *J. Clin. Investigation* **26**:1175, 1947.
18. McIndoe, A. H. Vascular lesions of portal cirrhosis. *Arch. Path.* **5**: 23-40, 1928.
19. Herrick, F. C. Experimental study into cause of increased portal pressure in portal cirrhosis. *J. Exper. Med.* **9**:93-104, 1907.
20. Dock, W. Role of increased hepatic arterial flow in portal hypertension of cirrhosis. *Tr. A. Am. Physicians* **57**:302-306, 1942.
21. Bradley, S. E., Ingelfinger, F. J., Groff, A. E., and Bradley, G. P. Estimated hepatic blood flow and hepatic venous oxygen content in cirrhosis of liver. *Proc. Soc. Exper. Biol. & Med.* **67**:206, 1948.
22. Groff, A. E., Baldwin, E. deF., and Bradley, S. E. Hepatic arteriovenous oxygen differences in patients with normal and diseased livers. *Federation Proc.* **7** (Part I):45, 1948.
23. Bradley, S. Effect of posture and exercise upon blood flow through liver. *Tr. Josiah Macy Jr. Foundation Conference on Liver Injury* **7**:53-56, 1948.

POST-PARTUM HEMATOMA*

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IN REVIEWING discussions on intra-partum and post-partum complications in the obstetric textbooks one finds little space allotted to hematomas. A survey of the literature discloses 188 cases of paravaginal hematoma reported from 1554 to 1948. The incidence varies from 1:1951 deliveries reported by Moschkow[1] to 1:7000 by De Lee.[2] The immediate vulvar type is the most common. In a review of 1250 deliveries 3 cases of hematoma were found: the first was vulvar, requiring removal of episiotomy sutures, evacuation of the clot and resuturing two hours after delivery; the second was vulvar, requiring removal of sutures, evacuation of the clot and resuture twenty-four hours after delivery; and the third, which was of the late paravaginal type, is reported below. Another group that has been separately reported is the retroperitoneal. Williams[3] reviewed 33 cases of this kind, 22 occurring prior to 1880, with a mortality of 73 per cent. De Lee[2] states that the mortality in this type was 40 per cent prior to the institution of active treatment. Hamilton[4] reported a mortality of 8.3 per cent since the introduction of active treatment, and Frank-Kamenetsky[5] one of 9.5 per cent.

Obstetric hematomas, then, may be vulvar, paravaginal, intraligamentary or retroperitoneal, or a combination of these locations. The vulvar type appears immediately or within a few hours after delivery, the bleeding vessel being located external to the pelvic fascia and levators. Later, a blue, sensitive, elastic mass appears, and the diagnosis is made on inspection and palpation. The paravaginal type may be unnoticed for some time. The patient complains of increasingly severe pain, "bearing-down" pains or rectal discomfort. On examination a mass may be found in the vaginal wall projecting into the vagina. On rectal examination a mass may be palpated. This is the type that can dissect upward beneath Poupart's ligament, into the broad ligament, and retroperitoneally to the diaphragm. Finally, with massive hemorrhage,

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the patient exhibits signs of shock, necessitating immediate supportive measures.

The etiology of this complication is quite apparent when one considers the progress of the fetus through the birth canal, subjecting the maternal tissue to long-standing contusing and avulsing trauma. And it is generally agreed that the immediate type is caused by trauma, which De Lee,[2] Hamilton[4] and others list as the major causal factor. The late type is attributed to pressure necrosis of vessels caused by prolonged compression by the fetal head. Also listed as causes are laceration of inelastic vessels, toxemias, the presence of a blood dyscrasia and varicosities. Even slight trauma may activate these cases. Lacomme[6] believes that hematomas may occur more frequently in the young primipara. The logic is apparent — the canal has not been previously dilated, and there is more tissue resistance. In general it may be said that the early hematomas are due to trauma and the late ones to pressure necrosis.

The diagnosis is made on the bluish discoloration, tumefaction and pain. Inspection and examination of any patient complaining of severe, continuous pain after delivery is mandatory. All reviewers stress the fact that cases are missed because the attending physician attributes the complaint of pain to episiotomy sutures. In the subperitoneal hematoma, tearing, labor-like pain continues, a high fundus is found, and early shock occurs.

Treatment should be prophylactic so far as possible. An episiotomy and the use of outlet forceps will help prevent vulvar damage, especially in young primiparas. A thorough inspection for tears and good tissue approximation are essential. Michaels and Herring[7] stress the importance of the repair, stating that an insignificant ooze at the upper angle of a tear or an episiotomy may in a few hours be a large hematoma. Early diagnosis[8, 9] and evaluation of the case is the next step. Expectant treatment is used when a small hematoma is discovered and does not increase under observation. A hematoma that is enlarging, or a hematoma that is large on discovery, should be incised and evacuated, and the bleeding controlled. This may be accomplished by suture, pressure, pack or hemostatic absorbable gauze, or a combination of these measures. If there has been severe hemorrhage, shock treatment is immediately instituted, blood replacement of course being most important. If infection is present, incision and drainage, culturing and the use of the most specific agent available are advisable. Immediate treatment with streptomycin and penicillin, while culture reports are awaited, seems a sensible plan.

In view of the early ambulation used in hospitals and the shorter hospitalization now popular, more late hematomas may be seen than in the past. The following case is presented with this consideration in mind.

Case Report

A 28-year-old bipara, 7 days post partum, reported to the accident room complaining of severe perineal pain. The discomfort had begun with activity at home after discharge from the hospital. Pain had become so severe that she could not sit comfortably. There had been bright-red vaginal bleeding for 2 days, and the patient had become weak and lightheaded. Her obstetrician stated that pregnancy and labor had been normal and that a median episiotomy had been done and a low forceps delivery effected without incident. The usual repair had been made. No lacerations had been observed, and no vulvoperineal mass or discoloration noted. The patient had apparently been in good condition on discharge.

The past history was noncontributory.

Physical examination revealed a hard, symmetrical mass extending about 10 cm. above the pubis. The inguinal lymph nodes were enlarged bilaterally, more so on the left. On vaginal examination marked perineal blueness was found, extending beyond the ischial tuberosity left laterally and into the labium, and to the anal margin inferiorly. A gaping episiotomy incision exuded serosanguineous material from two openings, each about 2.5 cm. in length. A moderate bloody vaginal discharge was present. Only one finger could be introduced into the vagina with comfort. A mass was found in the left wall about 7 cm. inside the outlet, extending superiorly to the fornix and nearly obliterating the vaginal canal.

The temperature was 104.4°F., the pulse 140, and the respirations 22.

The urine showed a trace of albumin. The red-cell count was 2,860,000, with a hemoglobin of 58 per cent, and the white-cell count was not elevated; the blood chemical findings were normal. The blood type was O, and the patient was Rh+.

The diagnoses were late post-partum vulvovaginal hematoma, infected, median episiotomy, infected, and secondary anemia.

General treatment consisted of transfusion, intravenous administration of fluids, penicillin and streptomycin until the culture report revealed colon bacilli, and then streptomycin alone for 4 days.

Local treatment was definitive, incision and drainage of the mass being accomplished under sodium pentothal anesthesia. At this time about 500 cc. of blood clot and dark, thick blood with a strong odor of colon bacilli was evacuated, a culture taken, and the cavity irrigated with physiologic saline solution. The cavity was found to extend to the peritoneal reflection, having dissected superiorly the length of the vagina, to the anal margin inferiorly, to beyond the ischial tuberosity left laterally, and beyond the site of the episiotomy medially. Drains were inserted through a stab wound medial to the left ischial tuberosity and through the wide open episiotomy wound. The cavity was packed through the vaginal incision, and a "T" binder was applied. Packs were changed and drains shortened in 24 hours. All drains and the vaginal sponge were removed on the 6th day. Potassium permanganate douches and sitz baths were then instituted until discharge on the 11th day.

Postoperative examinations revealed excellent general healing and the presence of a painful scar at the site of the episiotomy along with a relaxed vaginal outlet. Excision of the painful cicatrix and perineorraphy were accomplished 4 months after the original operation. The patient left the hospital in 8 days. Follow-up examination showed a well healed, firmly supported perineum. The vagina admitted 2 fingers without discomfort. No pelvic abnormality was noted.

Summary

A review of the literature from 1554 to 1948 reveals 188 cases of paravaginal hematoma.

Obstetric hematomas may be immediate or late and are anatomically classed as vulvar, paravaginal, intraligamentary or retroperitoneal, or a combination of these locations.

Early diagnosis and immediate active treatment are advisable because of the high mortality in severe cases.

A case of late post-partum vulvovaginal hematoma, exemplifying many of the points considered, is presented, and its treatment described.

References

1. Moschkow, B. N. Das Hämatom der Geburtswege. *Monatschr. f. Geburtsh. u. Gynäk.* **92**:421-437, 1932.
2. De Lee, J. B., and Greenhill, J. P. *The Principles and Practice of Obstetrics.* Ninth edition. 1011 pp. Philadelphia: W. B. Saunders Co., 1947.
3. Williams. Cited by Davis, C. H. *Gynecology and Obstetrics.* 3 vol. Hagerstown, Md.: Prior Co., 1940. Vol. I. Chap. 24. P. 15.
4. Hamilton, H. G. Post-partum labial or paravaginal hematoma. *Am. J. Obst. & Gynec.* **39**:642-648, 1940.
5. Frank-Kamenetsky, C. Haematoma vulvae. *München. med. Wchnschr.* **56**:2028, 1909.
6. Lacomme, M. À propos des hématomes périvaginaux. *Médicine* **14**: 289-293, 1933.
7. Michaels, J. P., and Herring, G. S. Postpartal hematomata of vulva and vagina: case reports. *New Orleans M. & S. J.* **95**:37-39, 1942.
8. Duckman, S., and Tortora, J. Postpartum paravaginal hematoma. *Brooklyn Hosp. J.* **5**:153-156, 1947.
9. Lubin, S., and Horowitz, I. Postpartum hematomas: report of 4 cases. *Am. J. Surg.* **63**:272-275, 1944.

MEDICAL PROGRESS

TUBERCULOSIS

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IT IS well nigh impossible for a single reviewer to encompass the entire field of tuberculosis, so vast are its ramifications. In a review such as this, one is forced to limit himself to the highlights of the year, and, even then, some significant contributions may be overlooked or touched upon only lightly.

The fact that tuberculosis mortality continues to show a gratifying decline cannot be overlooked. The death rate for tuberculosis, with few interruptions, has shown a continuous decline since 1910. In 1946, it was only 36.4 per 100,000 population,[1] which amounted to a 9.2 per cent decrease from the rate of 40.1 in 1945. In 1947 the death rate had dropped to 33 per 100,000,[2] and, according to the Metropolitan Life Insurance Company,[3] a record low mortality may have been set in 1948. For their policyholders, the tuberculosis death rate declined from 32.3 per 100,000 in the first half of 1947 to 28.4 in the first six months of 1948, representing a reduction of 12 per cent. On the debit side of the ledger is the fact that in 1947 nearly 50,000 persons in this country still died of tuberculosis, nearly half of them between the ages of fifteen and forty-four. Although the over-all statistics are heartening, the time for complacency is still far off.

Streptomycin

So much additional evidence has accumulated during the past year for supporting the belief that streptomycin has a favorable influence on the course of tuberculosis as to dispel any doubt about its value. By far the largest series of cases treated with streptomycin is that reviewed by the Veterans Administration and the Army and Navy[4] and their "current status" report is well worth reading. In summary, it may be said that some degree of benefit may be expected regardless of the site of infection or organs involved. In pulmonary tuberculosis, "streptomycin, in conjunction with bed rest, has been demonstrated to reverse the trend of progressive predominantly exudative moderately and far advanced disease in a formidable majority of cases." In cutaneous sinuses and fistulas, streptomycin has demonstrated a "striking usefulness." Although the end results in tuberculous meningitis and miliary tuberculosis are not quite so good as had been anticipated on the basis of the patients' initial responses, treatment with streptomycin is "mandatory" in these cases. Bone and joint lesions and urogenital lesions show a slow response to streptomycin, and the combination of surgery and antibiotic therapy is indicated in these cases. The results of treatment of lesions of the alimentary tract are "uniformly and remarkably favorable." For all forms of tuberculous peritonitis, streptomycin is regarded as an effective remedy. Since the drug brings about improvement in 80 to 90 per cent of cases of tracheobronchial and laryngeal tuberculosis, it should be considered as a prime form of therapy in such patients.

Aside from these generalities, probably the most notable advance clinically is the demonstration that the relatively high doses of streptomycin previously employed can be reduced to lower, less toxic, levels without any appreciable impairment in effectiveness. Along with this, there has been a gradual reduction in the cost of the drug so that it is now more readily available to noninstitutionalized as well as institutionalized patients. An amount of 1 gm. daily in two divided doses at twelve-hour intervals for a period of one hundred and twenty days appears to be adequate, and 0.5 gm. daily for as short a period as forty-two days may prove to be effective in some cases. If the latter scheme proves successful, toxic reactions from streptomycin may be reduced to the vanishing point.

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When the therapeutic possibilities of streptomycin were first being explored it was wisely decided that additional measures other than bed rest had best be withheld so that any decision about the effectiveness of the drug would not be beclouded by other factors. Since streptomycin has already proved its effectiveness, this phase of evaluation can be said to be completed, and the time has now come when strict scientific evaluation is of less concern than the necessity of providing the patient with every form of treatment that will rid him of bacilli and restore him to health as quickly as possible. One may thus see streptomycin being given simultaneously with usual collapse treatments and, although such varied forms of therapy may be difficult to evaluate from the scientfic standpoint, there is reasonable likelihood that the period of the patient's disability will be reduced. Streptomycin therapy is rarely definitive in the sense that it often does not produce complete clearing of the tuberculous lesions and that a considerable percentage of relapses occur. "Its most frequent usefulness appears, therefore," comments the committee,[4] "to lie in conjunction with collapse therapy." The judicious use of streptomycin often makes collapse therapy a possibility in cases in which collapse would heretofore have been impossible or unlikely for one reason or another. According to the committee, the optimum time to induce collapse is during the first weeks of streptomycin therapy before resistance develops in the bacilli. From a practical standpoint, any patient with tuberculosis should receive any and all therapeutic measures, antibiotic and collapse, after a short period of observation has demonstrated their need.

Since the toxicity of streptomycin has been significantly reduced through the simple expedient of lowering of the average daily dose, only one significant drawback remains to its greater effectiveness. That drawback is the development of resistance (or, better, loss of sensitivity) of tubercle bacilli to the drug in some patients under treatment. Development of resistance is perhaps the chief reason for *not* using streptomycin in minimal lesions. In such cases the antibiotic is generally withheld since the prognosis is usually favorable without it, and, besides, should treatment with streptomycin become necessary at a later date, the drug would prove ineffective if loss of sensitivity had taken place. The increased resistance to streptomycin can be considerable and may be as high as a thousand times or higher. As a matter of fact, a curious paradox has recently been reported in the recovery from a patient of a strain of tubercle bacilli whose growth was considerably *enhanced* by the presence of streptomycin in the culture medium. The patient from whom this organism was isolated had been receiving the drug for ninety-six days for a pulmonary infection. In some cultures it was found that growth occurred in the presence of as much as 100 microgm., whereas no growth was evident on the medium without streptomycin.[5]

The development of a loss of sensitivity of the tubercle bacillus during streptomycin therapy has recently been studied in a joint program of the Yale University School of Medicine and the Laurel Heights Sanatorium under the auspices of the American Trudeau Society.[6] These studies are worth noting, for they are fairly typical of the universal experience in the development of resistance. A group of 16 patients with pulmonary tuberculosis were treated with 1.6 gm. of streptomycin in six divided doses for a period of four months. Sputums or gastric washings were collected at routine intervals, and tubercle bacilli were isolated by culture from these specimens. After growth had been obtained, transfer of part of a suitable colony was made to a tube of modified Dubos–Davis medium for in vitro sensitivity tests. It was found that in all 16 cases, the strains of the bacilli isolated prior to treatment were highly sensitive to streptomycin. Loss of sensitivity (tenfold increase in resistance) began to appear by the end of the first month of therapy, together with conversion of positive sputum or gastric washings to negative in other cases as determined by culture. By the end of the third or fourth month of therapy, cultures were positive in only 9 of the 16 cases. Sensitivity tests of the organisms from these positive cultures indicated that all the organisms had developed a tenfold or greater increase in resistance. Five of these nine strains developed a tenfold to fiftyfold increase in resistance; in the remaining four strains the increase was a hundred to greater than two thousand times.

How streptomycin resistance can be a cause of therapeutic failure is graphically illustrated by a case of miliary tuberculosis reported by Muschenheim, McDermott and Bunn.[7] The patient was a twenty-one-year-old man whose miliary tuberculosis was associated with cervical and mediastinal lymphadenitis of an extreme degree. Tubercle bacilli isolated from this patient were initially sensitive to less than 1 microgm. of streptomycin per cubic centimeter of medium in vitro. With the institution of streptomycin therapy (3.0 gm. daily), fever subsided, the superficial lymph nodes began to shrink visibly, stupor disappeared, the appetite became normal, and a rapid gain in weight ensued. For five weeks the patient seemed to be in complete remission. At that time, resistance of the organisms to streptomycin developed so that all the original symptoms returned with increased severity, and cultures of the tubercle bacilli revealed that the organism was now resistant to concentrations of streptomycin in excess of 1000 microgm. per cubic centimeter. The temperature became elevated, the downhill course was progressive, and death ensued seven weeks after the clinical onset of the relapse and five months after the institution of treatment.

Considerations of this type temper one's enthusiasm for the drug and certainly provide good reasons for not using it in the early, minimal case of uncomplicated pulmonary tuberculosis whose prognosis is usually favorable on bed rest or collapse therapy. This experience further indicates that the action of streptomycin is still to be regarded as *suppressive* rather than curative.

Since streptomycin is far from an ideal therapeutic agent, some efforts are being made to use other therapeutic substances along with streptomycin for possible synergistic effect. One such agent being explored is para-aminosalicylic acid (PAS). Youmans and his co-workers[8] have found evidence that such a synergism between streptomycin and PAS exists in mice, although it was possible to recover viable tubercle bacilli from all the mice treated regardless of the intensity of the therapeutic schedule. They note further: "Since the usefulness of para-aminosalicylic acid for the treatment of clinical tuberculosis is not known, the importance of these results in relation to the treatment of clinical tuberculosis can only be a subject for speculation." McClosky, Smith and Frias,[9] on the other hand, have carried out extensive researches on the toxicity, fate in the body and therapeutic efficacy of PAS in rabbits and guinea pigs. In these animals PAS had but little therapeutic effect by itself, and, when combined with streptomycin, it showed no more than a summation of effects without any indication of potentiation. In the light of these experiments, the value of PAS for human beings is doubtful.

Better results both experimentally and therapeutically have been obtained when streptomycin is combined with a sulfone such as promin or promizole. According to some investigators,[10] promizole can be given for a period of years without any apparent major toxic effects. Promizole seems to have an inhibitory action on hematogenous tuberculosis although clinical evidence of its action is usually delayed until at least six weeks after the drug is first given. According to this concept, if streptomycin and promizole are given together, a prompt action is obtained from the streptomycin and a more delayed effect is obtained from the promizole. Considerations of this nature prompted Lincoln, Kirmse and DeVito[10] to give this combination of drugs to 7 patients suffering from tuberculous meningitis. Promizole was administered orally in a total daily dosage of 0.5 to 1.0 gm., and this dose was gradually increased until a blood level of 2 to 3 mg. per 100 cc. was obtained. The streptomycin was given in doses of 0.5 to 2.0 gm. intramuscularly, and, besides, all patients received 0.1 gm. intrathecally daily at least during the first week of treatment. On this plan of management 6 of the patients survived and were apparently well three to eight months after institution of treatment. This is a remarkably good record for a disease as terrible as tuberculous meningitis, although the authors are well aware of the fact that their patients have not been under observation for a sufficiently long period to be considered "cured."

Deserving of some mention is the report by Slotkin[11] in which streptomycin therapy is combined with injections of an ethyl ester of chaulmoogra oil. This author believes that the fatty capsule of the tubercle bacillus can be dissolved by the chaulmoogra esters, and thus the organism may be rendered more susceptible to the action of the antibiotic. A brief experimental and clinical experience on urogenital tuberculosis is cited in the preliminary report, but many more data are necessary before this form of therapy can be extended more widely into clinical practice. One direction that experimental investigation might take is suggested by the studies of Karlson and Feldman[12] on the subeffective dose of streptomycin in experimental tuberculosis in guinea pigs. These investigators wisely point out that in a study of the effect of two or more chemotherapeutic agents on an experimental infection, it is necessary that the dose of each drug be low enough so that one of the drugs alone will not be responsible for the total therapeutic response. As far as guinea pigs are concerned, their results indicate that if the daily dose of streptomycin is kept at 2.0 mg., it may be considered as being subeffective and suitable for testing the additive or synergistic action of other compounds.

Pneumoperitoneum

During the past few years pneumoperitoneum has definitely emerged as a valuable form of collapse therapy on a par with pneumothorax if not actually surpassing it in many cases. Banyai,[13] one of the pioneers to use this form of treatment as far back as 1931, has recorded his experiences and that of others in considerable detail. Mitchell and his colleagues,[14] in North Carolina, have summarized the literature since 1937 in convenient tabular form and have described their own experience with this procedure, which covers 703 patients, 474 of whom were treated for three months or longer. Although they do not regard their results as offering "final proof of the efficacy and safety of pneumoperitoneum," they believe that pneumoperitoneum may be preferable to conventional collapse therapy or simple bed rest in cases with fairly extensive, predominantly productive disease with positive sputum provided the cavities are not too old or thick walled. If pneumoperitoneum is used in conjunction with phrenic paralysis, it is best to start pneumoperitoneum prior to surgery because with it one gains valuable information about the mobility of the diaphragm and its attainable elevation. In their own experience, Mitchell et al.[14] found that the use of pneumoperitoneum for an average of fifty-four and a half weeks was responsible for 57 per cent satisfactory

results in 188 white patients and in 37 per cent of 286 Negroes, all of whom were "not amenable to conventional forms of collapse therapy."

Since pneumoperitoneum is a relatively new procedure, exact definition of its indications and contraindications is lacking. According to Aronovitch, Caswell and Zadé,[15] the indications for pneumoperitoneum may be summarized as follows: moderately advanced bilateral tuberculosis when artificial pneumothorax cannot be given; unilateral disease in which pneumothorax is impossible for one reason or another; to supplement phrenic crush; as an adjunct to artificial pneumothorax; as a preliminary measure in early bilateral cases; and for basal lesions with or without cavitation. Of 42 cases (1800 refills) carried out by this group, improvement was noted in 24, or 57 per cent, and there were no major complications.

Pneumoperitoneum has many advantages over conventional pneumothorax, some of which are listed by Anderson.[16] Pneumoperitoneum does not interfere with the normal physiology of the intrapleural space in the way that pneumothorax does, and it does not create thickening of the pleura or produce an unexpandable lung. In bilateral disease, pneumoperitoneum has the advantage that both lungs can be collapsed by one injection of air. A further advantage is that the underlying lung can be visualized while treatment is continuing, and progress can be followed better than with pneumothorax. Pneumoperitoneum is a reversible procedure — one that can be induced, discontinued and reinduced almost at will. Spontaneous pneumothorax and bronchopleural fistulas are avoided. Anderson[16] states:

> Perhaps the outstanding advantage of artificial pneumoperitoneum over artificial pneumothorax, as far as the general practitioner is concerned, is the fact that fluoroscopic control is not essential. The operator simply injects enough air to inflate the abdomen snugly. He need not worry whether he is puncturing the lung, collapsing it too far, or losing the space — any of which complications may occur with artificial pneumothorax.

Fluoroscopic guidance is always valuable, however, even though it may not be essential in every case. Further experience will, of course, be necessary to determine whether pneumoperitoneum is preferable to pneumothorax in the outpatient or ambulatory management of tuberculous patients.

Complications with pneumoperitoneum are less frequent than with pneumothorax, but complications may occur. Air embolism is a possibility,[17] and death from this complication has been noted.[18] Sterile peritoneal effusions occur in about 8 per cent of the cases, and although they may require paracentesis, they do not necessarily indicate the abandonment of the pneumoperitoneum. On the other hand, peritonitis, either tuberculous or pyogenic, may be a serious complication and may necessitate discontinuation of pneumoperitoneum and the institution of suitable chemotherapy or antibiotic therapy. Peritoneal adhesions may be seen in a great number of cases roentgenologically, but they seldom cause trouble. Penetration of abdominal viscera is a complication that is dreaded by beginners but is one that seldom occurs. Subcutaneous emphysema is a readily avoidable complication.

Although the technic of inducing and maintaining pneumoperitoneum varies somewhat from operator to operator, it is admittedly more simple than pneumothorax. Induction is usually carried out in the left lower quadrant under local procaine anesthesia, and the details can be found in any of the recent articles cited above. The amount of air given at the initial injection varies from 400 to 800 cc. and refills, at intervals of seven to fourteen days, amount to anything from 500 to 1500 cc. or more. Positive pressures are used, and the final pressure is kept under 20 mm. of water, the average being 12 to 16 mm. There is no fixed rule in this respect, and individual variability must be taken into consideration. Manometric readings in pneumoperitoneum do not have the precise significance that they have in pneumothorax.

Although thousands of patients have been treated by pneumoperitoneum most of them have received treatment within the past few years, and suitably long follow-up material is not available. Trimble et al.[19] have studied quite carefully 407 consecutive cases, of which 382 were adequately followed. In this latter group arrest of the disease was possible in 57 per cent, and an additional 13 per cent were definitely improved. It is to be noted that in their patients, arrest was achieved in 82 per cent of the minimal cases, in 79 per cent of those that were moderately advanced, and in 39 per cent of the far-advanced cases. Of 233 patients with cavitation, 47 per cent became arrested, and another 18 per cent were definitely improved. These results are at least as good as, if not better than, those in any comparable series treated by pneumothorax.

A recent editorial by Howlett[20] presents a sound appraisal of the present status of pneumoperitoneum without any bias or prejudice. He points out that there is still great divergence of opinion regarding the indications, effectiveness and usefulness of pneumoperitoneum in spite of the fact that it has been used for more than a decade. At present, he says, pneumoperitoneum seems to be heading for its phase of rapid expansion as a form of treatment, and, without doubt, some disillusionment with it will develop, especially when it comes to be used in forms of the disease in which it is not effective. Furthermore, as pneumoperitoneum ascends in vogue, it will be employed by more and more operators who are not adequately trained either in its administration or in the evaluation of the cases in which it may not be indicated. On the other hand, Howlett admits that he knows of no case "in which a physician has used pneumoperitoneum adequately

on enough patients for a sufficient period of time and has then discarded it as a procedure of no value." The chief danger of pneumoperitoneum, he believes, is not the procedure itself but the ease with which it may be given and the fact that the readiness with which it is tolerated by most patients may lead to its indiscriminate and excessive use. Howlett's editorial should be read by everyone attempting to perform pneumoperitoneum, especially the beginner.

Sporadic reports have appeared about the possible usefulness of pneumoperitoneum in the treatment of bronchial asthma. Attention is again called by Rubin and Gass[21] to a case of intractable asthma that responded to this form of therapy. It is interesting to note that in the reproductions of the roentgenograms that accompany the article, considerable basal emphysema is present and that the amount of pneumoperitoneum used seems to be less than is customarily employed in the treatment of tuberculosis. Further investigation on the use of pneumoperitoneum in such cases is definitely indicated.

BCG

Evidence continues to accumulate that BCG (Bacillus Calmette–Guérin) is a safe and relatively efficacious vaccine for the control of tuberculosis. The policy of the American Trudeau Society[22] regarding its use can be briefly summarized as follows: the degree of protection afforded by BCG is neither complete, nor is the duration of the induced immunity permanent or predictable. Nevertheless, it is recommended that the immunization be made available to medical and hospital personnel who are exposed to infectious tuberculosis, persons who are unavoidably exposed to infection in the home, inmates and employees of various institutions such as mental hospitals and prisons, and others who are considered to have a low resistance to tuberculosis and who live in communities in which the tuberculosis mortality is high. Vaccination of the general population is not recommended at present except under certain carefully controlled conditions. It is also not recommended that the vaccine be made available for general distribution since there is still some uncertainty about the most effective strain of BCG to be used and the most effective method of vaccination. It is the belief of the American Trudeau Society that the most effective methods of controlling tuberculosis are those already established, such as more intensive case-finding, segregation, intensive therapy and rehabilitation. BCG is not a substitute for approved hygienic procedures. A similar opinion regarding BCG is held by the United States Public Health Service.[23, 24] It is perhaps unnecessary to add that BCG should only be given to persons who are negative reactors to tuberculin.

It is interesting to compare the limited experience with BCG in this country with that obtained elsewhere. In Scandinavia[25] vaccination with BCG has been established as a public-health measure since 1926, although it is by no means the only antituberculosis weapon employed. Other measures, such as tuberculin surveys and x-ray examinations, are intensively conducted, and, with such a vigorous program, the tuberculosis mortality in these countries has been reduced from 250 per 100,000 population in 1900 to less than 70 in 1944. So favorable were the early results with BCG that a national BCG laboratory was established in Norway in 1936, and, subsequently, BCG vaccination became obligatory for all tuberculin-negative student nurses. With the cruel German occupation of Norway in 1939, large numbers of tuberculin-negative young people were crowded into small and unhygienic quarters, and epidemics of tuberculosis were reported in all parts of the country. Political interference forced BCG vaccinations to be given surreptitiously, and yet, in spite of all these difficulties, the statistics at the end of this unhappy period indicated a "very considerable immunizing efficiency of the vaccine."

In Sweden, all medical students and pupil nurses are now tested before beginning hospital service, and the nonreactors are vaccinated.[26] Conscripts in the services are vaccinated at the beginning of their term of service, and so are the majority of school children in the last class of primary school. In the city of Örebro the whole population has been tested, and the nonreactors have been vaccinated with BCG. All newborn babies are also vaccinated. On the basis of this experience, Malmros[26] urges BCG vaccination as a part of any modern tuberculosis program. He further advises that all vaccinated persons be checked at stated intervals and that those who have become tuberculin negative be revaccinated.

In this country, the most extensive experience with BCG is that reported by Aronson,[27, 28] of the Office of Indian Affairs, and by Rosenthal and his colleagues[29] at the Municipal Tuberculosis Sanatorium in Chicago. Some of the statistics of the former investigator have been previously reviewed.[30] The latter group has performed extensive laboratory investigations on BCG and conducted a study of the effects of vaccination on the following six groups of patients: newborn infants at the Cook County Hospital; medical students at the University of Illinois; infants born of tuberculous parents anywhere in Chicago; student nurses at the Cook County Hospital; children at a federal housing project; and inmates of a mental institution. Their studies, which have been in continuous operation for thirteen years, constitute the longest continuous experiment on BCG vaccination in the United States.

It can be said that these clinical experiments have proved reasonably successful. Of 2831 newborn

infants who were not in household contact with tuberculosis, there were 11 cases of tuberculosis in the vaccinated as against 39 in the controls. One death was recorded in the vaccinated, and 7 in the controls. In 1159 siblings the tuberculosis rate per thousand was five times as great in the controls as in the vaccinated. Among 256 newborn infants, when tuberculosis was present in the household and when isolation in foster homes was practiced in the controls and in the vaccinated alike, there were 2 cases of tuberculosis in the vaccinated as compared with 5 in the controls. In the federal housing project 699 children were vaccinated, 625 controls did not react to tuberculin, and 275 reacted to tuberculin and were not vaccinated. Considering the negative and positive reactors not vaccinated, there were 7 cases of tuberculosis, of which 2 were fatal, against no cases of tuberculosis in the vaccinated group. It was found that subsequent to vaccination a positive tuberculin test persisted as long as six years in the great majority of the children. Additional studies by Neiman and Loewinsohn[31] have suggested that BCG inhibits the development of primary as well as secondary tuberculosis in infants. Their investigation, which is based on a study of 13,470 chest roentgenograms, furnishes additional proof of the efficacy of BCG.

Since successful vaccination with BCG converts a negative reactor to positivity, the vaccine should not be used in areas where tuberculosis mortality and morbidity are low and where tuberculin negativity is prevalent. The chief exponent of this viewpoint is Myers,[32] who has repeatedly pointed to the admirable accomplishments in Minnesota, where tuberculosis has been largely eradicated. This has been achieved without the use of vaccination and through rigid adherence to sound public-health principles. To quote from Myers:

> The tuberculin test is our only refined epidemiological agent. Indeed, it is only through its continued use that total eradication can be achieved. So-called immunizing substances, such as BCG and the vole tubercle bacillus, which sensitizes the tissues to tuberculoprotein, could serve no purpose except as a smoke screen for the tubercle bacillus in Minnesota. If used, they would nullify our most effective weapon — the tuberculin test. Moreover, their efficacy even in tuberculosis control has never been proved in any sense of the word. They remain in the same position as their dozens of predecessors, namely, the theoretical and experimental stage. In parts of the world where BCG has been used, no achievement in tuberculosis control has been reported that even remotely approaches that in the United States, where sound epidemiological methods have been in vogue.

It is obvious, however, to the critical student of the subject that the situation in the United States, where "sound epidemiological methods" have been allowed to flourish unhampered by war, is entirely different from that in the devastated nations of Europe or some of the backward countries of South America. Even in the United States the situation in Minnesota may be likened to a safety zone that lies in the midst of streaming traffic. To carry the analogy a bit farther, the wise Minnesotan will remain on his little island if he wishes to retain his health. To travel abroad without any immunity might prove particularly hazardous. Of course, if he so desired, he might remain where he is until traffic around him quieted down, but that might take a good many more years. In brief, Myers's argument applies very well at the present time to Minnesota. It does not, as yet, apply to the rest of humanity.

Bacteriologic Considerations

Although there has been a constant interest in the discovery of improved methods for culturing tubercle bacilli, there is no doubt that this interest was given considerable impetus by the reports of Dubos[33] and Dubos and Davis[34] on the use of liquid mediums for the rapid and submerged growth of these organisms. So reliable are the cultural methods at the present time that they have to a large extent replaced the more costly animal tests. Cultural methods have the additional advantage that they are superior in disclosing not only small numbers of virulent mammalian bacilli but also tubercle bacilli of low or moderate virulence. According to Corper and Bain,[35] the chief advantage of the animal test is that it overcomes the problem of eliminating the undesirable contaminating organisms without injury to the virulent tubercle bacilli. They have found, however, that by the use of trisodium phosphate in the culture medium, this disadvantage of the culture method is largely overcome.

The Dubos medium is being used widely for the culture of material obtained directly from the patient for the identification of tubercle bacilli. Goldie[36] reports that of 400 sputums examined by this method 34 were positive by culture and negative by smear. He states that compared with other culture methods, "the use of the Dubos medium is inexpensive, easily learned by an average technician, suitable for daily examinations of a large number of specimens, and, what is more, offers the advantage of a rapid (within 8 to 15 days) culture diagnosis of sputa containing relatively small numbers of *M. tuberculosis*." Foley[37] has studied 197 specimens obtained from various sources by both culture and inoculation methods. He believes that the method is valuable but points out that saprophytic mycobacteria from urine and gastric contents as yet cannot be sufficiently differentiated from tubercle bacilli for the exclusive use of these mediums for the specific diagnosis of tuberculosis. In these cases animal inoculation studies must be done for positive identification of the organism.

Cultural methods are of value not only in detecting tubercle bacilli but also in testing various antibiotic and chemotherapeutic agents. Although many such reports have appeared in the literature in the past year, only one is cited here as being illustrative of its value. Wong et al.[38] have noted

that the earlier attempts to demonstrate any antibiotic activity of subtilin in vitro by use of Long's synthetic medium have ended in inconclusive results. They therefore tested subtilin against a suitable strain of human virulent tubercle bacilli in Dubos medium and found that under the conditions of the test a 1:400,000 dilution of subtilin regularly inhibited the growth of these organisms and that dilutions of 1:20,000 were bactericidal. Rapid testing of new antituberculosis substances can thus be achieved through the use of the Dubos medium. The simple medium of human blood and glycerin, described by Dunphy and Fousek,[39] may also prove valuable in this direction.

Arguments have appeared from time to time supporting the use of alcohol as a disinfectant for both tubercle bacilli and other micro-organisms. The latest contribution to this argument is that presented by Smith,[40] and it is worth the attention both of private practitioners who have occasion to deal with tuberculosis and of hospital administrators. Smith cites extensive literature of this subject and his own many experiments. He finds alcohol to be an effective disinfectant against tubercle bacilli if attention is paid to the type of contamination and the concentration of the alcohol employed.

Surgical Considerations

In recent years the indications for pulmonary resection have come to be clarified and the procedure standardized in much the same way as thoracoplasty. According to Moore[41] the indications for resection of tuberculous lungs include thoracoplasty failure, basal disease that fails to respond to conservative measures, endobronchial disease associated with tension cavities or pulmonary suppuration, tuberculoma and the so-called "destroyed lung" with extensive caseation and cavitation. Moore believes that the contralateral lung should be comparatively free from disease, or that any existing focus should be relatively stable or arrested. He further states that he can see "no sensible reason why the operation should be attempted in patients who have had bilateral disease and whose vital capacity is so low that pulmonary resection leaves them hopeless cripples, even though it may convert their sputum to negative."

At present, as Clagett and Seybold[42] point out, the greatest hazard to patients with tuberculosis undergoing resection is late spread of the disease. This problem of late spread or reactivation has plagued every thoracic surgeon, and, in every case, statistical surveys of late results are found to be definitely inferior to the immediate mortality or morbidity. This is understandable for two reasons: tuberculosis is a generalized disease, and the removal of the most obvious focus does not rid the patient of his infection or alter his immunologic reaction to the tubercle bacillus; microscopic amounts of "spilling" during the operation into the unresected lung may not be immediately noticeable, and yet the organisms have been "planted" only to make their visible appearance at a later date.

The limited and restricted role that resection must play in the treatment of tuberculosis is brought out in the figures cited by Clagett and Seybold.[42] Of 29 patients operated upon in their series (14 cases of lobectomy and 15 of pneumonectomy) 19 were clinically well and had sputum free of tubercle bacilli. Four patients were dead, 5 had active disease, and 1 was untraced. Sweet[43] also finds that the late results of resection are inferior to the immediate results and urges that at least one year be allowed to elapse before any report is made regarding such surgical procedures. He notes that of the 6 cases of lobectomy reported by Churchill and Klopstock in 1943, only 4 can be said to have done well three years later, and 3 of these 4 would probably have done equally well under thoracoplasty. "What appear to be very encouraging results at first," says Sweet, "have many times turned out to be disappointing when appraised some months later." He points out that of 13 reactivations following lobectomy (in a total of 27 cases), 11 occurred as a late complication. Of 10 reactivations after pneumonectomy (in a total of 36 cases), 7 were of late occurrence. It is important to note that Sweet's study includes only patients operated upon prior to the advent of streptomycin. It seems likely that streptomycin will minimize these complications, but it should also decrease the necessity for such radical surgery.

Perhaps the most enthusiastic proponents of lobectomy and pneumonectomy as a surgical treatment of tuberculosis have been Overholt and his group.[44] They believe that many of the patients for whom these procedures have been performed are "desperate-risk" patients whose death might otherwise have been anticipated with great certainty. "We feel," they say, "that *any salvage in this group of patients, regardless of how small, can be considered pure gain.*" Their analysis of 88 patients treated by 92 resections and followed from two to twelve years shows that 68 patients could be considered as reasonable risks and 24 were desperate risks. Among 58 patients treated by pneumonectomy, there were 13 deaths in the sixty-day postoperative period and 11 late deaths, making a total case fatality of 41 per cent. Among 33 patients treated by lobectomy, there were 3 postoperative deaths and 3 late deaths. Only 14 of the 33 were clinically well and had consistently negative sputum. It must be noted that these statistics, too, antedate the use of streptomycin.

That streptomycin is a drug of much benefit in the management of surgical patients is already borne out by experience. What effect the drug will have on the incidence of late spreads, however, is still not known. Glover et al.[45] have cited their experience with streptomycin in conjunction with resection,

and their results, to date at least, are encouraging. They suggest that prophylaxis against immediate spread may be obtained and some other surgical complications may be reduced by streptomycin, and the doses needed to accomplish this may be smaller than those generally required for therapy. They believe that if the surgical mortality can be further reduced by a decrease of such complications, the indications for radical surgical treatment will be broadened. It seems to me, however, that although the *indications* may be broadened by the use of streptomycin, the over-all necessity for radical surgery may be reduced.

It may be well in this discussion of surgery to call attention to two procedures or technics that may prove of value in certain cases. The first is decortication of the lung in organizing hemothorax and empyema. In these cases the lung is bound down by a thick shell of fibrinous membrane that severely restricts respiratory activity. In certain cases it is possible to peel this membrane off, and one can then actually see the lung re-expand to fill completely the thoracic cavity. Lowe[46] reports 3 cases in which the decortication procedure was performed, in 1 of which the patient had tuberculous pleurisy and atelectasis. The postoperative course was excellent, and the patient gained weight and was relieved of his respiratory disability.

The second technic worth mentioning is the use of lucite spheres that are inserted into the thorax to assist in collapsing the lung in some cases of extrapleural pneumonolysis. Cases chosen for this procedure are those that would ordinarily be considered candidates for thoracoplasty, but the procedure has the advantage of less chest deformity. Although the indications for this operation are reasonably well established, it should be pointed out that there is only one year's experience and 30 operated cases behind this method and that it would be well to follow these patients for a longer period before the exact role of lucite plombage in the treatment of pulmonary tuberculosis can be evaluated. The authors[47] are themselves cognizant of this fact and make note of it in their paper.

Rehabilitation and Psychiatric Aspects

It is safe to say that there has been more nonsense written about rehabilitation as it pertains to tuberculosis and about the mental attitude of tuberculous patients than there has been on any other phase of this complicated disease. Some of this stems from the fact that each specialist, be it social worker, rehabilitation expert or epidemiologist, is so concerned with his small specialty that he fails to see the forest because of his emphasis on an individual tree. Clinicians, too, have been accused of looking too closely at the patient's lungs to the exclusion of the body and soul in which the lungs are but a small part. Nevertheless, it does not follow, as some have suggested,[48] that the clinician has to be "assisted by medical social workers, institutional and public health nurses, occupational therapists, and librarians . . . to realize the total portrait of the drives and dreams of the men and women who submit themselves to his care." Any good doctor does all that in his daily handling of his patients.

Pinner[49] points out that reports on the final results of rehabilitation are still too few to be significant. He states:

> That rehabilitation work is a necessary and important part of the successful treatment of many patients is quite generally accepted; it has come into its own during the last quarter of a century, in word and program, if not in action and reported results. . . . If advocates of any medical or surgical treatment of tuberculosis had, for twenty or even ten years, written profusely on plans, methods, set-ups, theory and — the philosophy (a beloved misnomer!) — of some treatment without publishing statistically acceptable reports of results in terms of numerically significant case reports, they would, by now, find their treatment pretty well discredited. But this is, in essence, the present status of rehabilitation work.

For those who are interested in detailed discussions on the psychiatric appraisal of the tuberculous person, two recent articles[50, 51] may prove helpful. The impression that one gains from these articles, however, is that the tuberculous patient is an exceedingly complicated person, buffeted by the storms of his emotions and anxieties. The implication is that many tuberculous patients should have the benefit of a psychiatrist in their routine management. As a matter of fact, another author[52] states:

> There is a real challenge to psychiatry in the coming years to contribute materially to the improvement of the tuberculous. To do this, there must be close co-ordination of effort between individuals and agencies dealing with tuberculosis and mental hygiene. With the appearance of national interest in the mental hygiene movement, and its sponsoring through federal and state appropriations, the means are now available for the formation of a unified program of medical, psychiatric and sociologic treatment of the patient with tuberculosis.

Yet, it seems to me, the problem is far less involved. After all, as Dufault[53] points out, the personality of the tuberculous patient is, on the whole, uncomplicated:

> He has his whims, his quirks, his idiosyncrasies, no doubt, but they run along the lines of yours and mine. He knows anger and resentment — and who does not? — but he is familiar with appreciation and gratitude. He can laugh or cry, smile or frown, talk or sulk, according to his moods. These are normal behavior traits which sound their harmonious or discordant notes in the shop and in the office as well as in the sanatorium.

It is well to note that this evaluation comes from one who has spent many years in the study of tuberculous patients and is not based on an "interview" that lasts an hour or two.

Perhaps the best of the recent discussions that deal with the psychology of the tuberculous patient is that by Moorman.[54] His experience in the treatment of the tuberculous has also extended over a great many years. Moorman believes that on a

broad psychosomatic basis every patient with tuberculosis is sick in mind as well as in body. That does not mean, however, that every victim of the disease needs the attention of a psychiatrist. "With rare exceptions," says Moorman, "the tuberculous patient needs only a wise phthisiotherapist who knows that mind and body are so interdependent that there can be no life when they cease to function as one." He adds that under ordinary circumstances the patient's interest should not be divided between several doctors, and his confidence in his attending physician should not be disturbed. On the average, the suggestion that a psychiatrist should be called to assist in the management of the case would only serve to spotlight the patient's mental aberrations "and aggravate his psychic conflict which otherwise might have resolved in the course of time almost, if not quite, unconsciously."

Since there is often a relation between the patient's mental state and the problem of irregular discharge from the sanatorium, the exhaustive study of such discharges by Tollen[55] is worth particular mention. Although his analysis of the situation is based on the experience of the Veterans Administration, the conclusions that he reaches have much wider applicability. It is apparent that a great deal of the responsibility of irregular discharges lies with the first physician who "breaks the news" to the patient that he has tuberculosis. The understanding and the reassurance that the patient receives from his doctor are far more important in creating a frame of mind conducive to successful hospitalization than any help the patient receives from others. In other cases, inadequate personal attention by the physician at the sanatorium is cited as a cause of premature departure of the patient from the hospital. Among the many suggestions that are made for correcting some of the evils that now exist, an excellent one is redefinition of the term "against medical advice." It is pointed out that if the staff doctor *knows* that a particular veteran requesting discharge will receive proper care at home and if no local health ordinance is violated, it should be unnecessary to discharge a patient "against advice" even though he still requires positive treatment for tuberculosis. Many other valuable suggestions are advanced by Tollen, and his article should be read by all sanatorium directors and their professional subordinates.

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References

1. Halpin, E. H. Tuberculosis mortality in United States, 1946. *Pub. Health Rep.* **63**:1029-1045, 1948.
2. Brophy, F. Why bigger Seal sale? *Bull. Nat. Tuberc. A.* **34**:118, 1948.
3. 1948 may set new low mortality record. *Statist. Bull. Metrop. Life Ins. Co.* **29**:3-6, 1948.
4. Council on Pharmacy and Chemistry. Streptomycin in treatment of tuberculosis: current status. *J. A. M. A.* **138**:584-593, 1948.
5. Spendlove, G. A., Cummings, M. M., Fackler, W. B., Jr., and Michael, M., Jr. Enhancement of growth of strain of *M. tuberculosis* (var. hominis) by streptomycin. *Pub. Health Rep.* **63**:1177-1179, 1948.
6. Sadusk, J. F., Jr., and Swift, W. E., Jr. Sensitivity of tubercle bacillus to streptomycin before and during specific therapy. *J. Clin. Investigation* **27**:278-282, 1948.
7. Muschenheim, C., McDermott, W., and Bunn, P. A. Streptomycin in clinical tuberculosis. *New York State J. Med.* **48**:889-894, 1948.
8. Youmans, G. P., Youmans, A. S., and Osborne, R. R. Combined effect of streptomycin and para-aminosalicylic acid on experimental tuberculosis in mice. *Journal-Lancet* **67**:403, 1947.
9. McCloskey, W. T., Smith, M. I., and Frias, J. E. G. Action of p-aminosalicylic acid (PAS) in experimental tuberculosis. *J. Pharmacol. & Exper. Therap.* **92**:447-453, 1948.
10. Lincoln, E. M., Kirmse, T. W., and DeVito, E. Tuberculous meningitis in children: preliminary report of its treatment with streptomycin and "promizole." *J. A. M. A.* **136**:593-597, 1948.
11. Slotkin, G. E. New and rapid method for control of urinary tuberculosis: preliminary report. *J. Urol.* **58**:464-478, 1947.
12. Karlson, A. G., and Feldman, W. H. Subeffective dose of streptomycin in tuberculous guinea pigs. *Am. Rev. Tuberc.* **58**:129-133, 1948.
13. Banyai, A. L. *Pneumoperitoneum Treatment.* 376 pp. St. Louis: C. V. Mosby Co., 1946.
14. Mitchell, R. S., et al. Pneumoperitoneum in treatment of pulmonary tuberculosis: results in 710 cases from 1937 to 1946. *Am. Rev. Tuberc.* **55**:306-331, 1947.
15. Aronovitch, M., Caswell, L. A., and Zadé, J. A. Pneumoperitoneum in treatment of pulmonary tuberculosis. *Canad. M. A. J.* **57**: 122-127, 1947.
16. Anderson, N. L. Artificial pneumoperitoneum in North Carolina. *North Carolina M. J.* **8**:706-710, 1947.
17. Hiatt, J. S., Jr., and Mitchell, R. S. Principles of pneumoperitoneum treatment of pulmonary tuberculosis. *North Carolina M. J.* **8**: 710-715, 1947.
18. Bailey, W. H. Air embolism in pneumoperitoneum: report of fatal case. *Am. Rev. Tuberc.* **57**:621-625, 1948.
19. Trimble, H. G., Eaton, J. L., Crenshaw, G. L., and Gourley, I. Pneumoperitoneum in treatment of pulmonary tuberculosis: 407 consecutive cases. *Am. Rev. Tuberc.* **57**:433-470, 1948.
20. Howlett, K. S., Jr. Pneumoperitoneum. *Am. Rev. Tuberc* **58**:134-138, 1948.
21. Rubin, J. H., and Gass, G. D. Pneumoperitoneum in treatment of bronchial asthma. *Canad. M. A. J.* **59**:162, 1948.
22. American Trudeau Society. Present policy of American Trudeau Society on BCG vaccination. *Am. Rev. Tuberc.* **57**:543-545, 1948.
23. Hilleboe, H. E. BCG vaccination: plans of United States Public Health Service. *Am. Rev. Tuberc.* **55**:294-296, 1947.
24. Weber, F. J. Further study of BCG vaccination. *Pub. Health Rep.* **63**:593, 1948.
25. Birkhaug, K. BCG vaccination in Scandinavia: twenty years of uninterrupted vaccination against tuberculosis. *Am. Rev. Tuberc.* **55**: 234-249, 1947.
26. Malmros, H. Late primary infection and BCG vaccination. *Am. Rev. Tuberc.* **56**:267-278, 1947.
27. Aronson, J. D. Present status of BCG vaccination in prevention of tuberculosis. *Pennsylvania M. J.* **51**:502-507, 1948.
28. *Idem.* Protective vaccination against tuberculosis with special reference to BCG vaccination. *Am. Rev. Tuberc.* **58**:255-281, 1948.
29. Rosenthal, S. R., Leslie, E. I., and Loewinsohn, E. BCG vaccination in all age groups: methods and results of strictly controlled study. *J. A. M. A.* **136**:73-79, 1948.
30. Wassersug, J. D. Tuberculosis. *New Eng. J. Med.* **235**:220-229, 1946.
31. Neiman, I. S., and Loewinsohn, E. Inhibition of primary tuberculosis by BCG: study in children based on 13,470 chest roentgenograms. *Am. Rev. Tuberc.* **56**:27-35, 1947.
32. Myers, J. A. Eradication of tuberculosis by epidemiological methods. *Am. J. Pub. Health* **38**:516-524, 1948.
33. Dubos, R. J. Rapid and submerged growth of Mycobacteria in liquid media. *Proc. Soc. Exper. Biol. & Med.* **58**:361, 1945.
34. Dubos, R. J., and Davis, B. D. Factors affecting growth of tubercle bacilli in liquid media. *J. Exper. Med.* **83**:409-423, 1946.
35. Corper, H. J., and Bain, W. Trisodium phosphate in diagnostic culture of tubercle bacilli. *Am. J. Clin. Path.* **18**:303-312, 1948.
36. Goldie, H. Use of Dubos medium for culture of *M. tuberculosis* from sputum. *Proc. Soc. Exper. Biol. & Med.* **65**:210-212, 1947.
37. Foley, G. E. Further observations on cultivation of tubercle bacilli from pathologic material in Dubos media. *J. Lab. & Clin. Med.* **32**: 842-846, 1947.
38. Wong, S. C., Hambly, A. S., Jr., and Anderson, H. H. Use of modified Dubos and Davis medium for demonstration of antibiotic activity of subtilin against *Mycobacterium tuberculosis*. *J. Lab. & Clin. Med.* **32**:837-841, 1947.
39. Dunphy, D. L., and Fousek, M. D. Simple medium for growth of tubercle bacilli. *Yale J. Biol. & Med.* **19**:1013-1015, 1947.
40. Smith, C. R. Alcohol as disinfectant against tubercle bacillus. *Pub. Health Rep.* **62**:1285-1295, 1947.
41. Moore, J. A. Pulmonary resection for tuberculosis. *North Carolina M. J.* **8**:715-717, 1947.
42. Clagett, O. T., and Seybold, W. D. Resection in pulmonary tuberculosis. *Proc. Staff Meet., Mayo Clin.* **23**:81-89, 1948.
43. Sweet, R. H. Lobectomy and pneumonectomy in treatment of pulmonary tuberculosis. *J. Thoracic Surg.* **15**:373-383, 1946.
44. Overholt, R. H., Wilson, N. J., Szypulski, J. T., and Langer, L. Pulmonary resection in treatment of pulmonary tuberculosis: analysis of 88 patients followed for period of two to twelve years after operation. *Am. Rev. Tuberc.* **55**:198-222, 1947.

45. Glover, R. P., Clagett, O. T., and Hinshaw, H. C. Streptomycin in resection in pulmonary tuberculosis: report of five cases. *Am. Rev. Tuberc.* **55**:418-427, 1947.
46. Lowe, E. S. Decortication of lung in organizing hemothorax and empyema. *U. S. Nav. M. Bull.* **48**:52-60, 1948.
47. Grow, J. B., and Dwork, R. E. Extrapleural pneumonolysis with lucite plombage. *Brit. J. Tuberc.* **42**:25-31, 1948.
48. Hilleboe, H. E. Rehabilitating tuberculous. *Pub. Health Rep.* **62**: 969, 1947.
49. Pinner, M. Rehabilitation and prognosis. *Am. Rev. Tuberc.* **56**: 165-167, 1947.
50. Ludwig, A. O. Emotional factors in tuberculosis. *Pub. Health Rep.* **63**:883-888, 1948.
51. Coleman, J. V., Hurst, A., and Hornbein, R. Psychiatric contributions to care of tuberculous patients. *J. A. M. A.* **135**:699-703, 1947.
52. Rossman, W. B. Psychiatric considerations in management of tuberculosis. *West Virginia M. J.* **44**:7-9, 1948.
53. Dufault, P. TB patients are people: role of psychotherapy in sanatorium wards should be major consideration of physicians as well as of psychiatrists and social workers. *Bull. Nat. Tuberc. A.* **34**: 123, 1948.
54. Moorman, L. J. Psychology of tuberculous patient. *Am. Rev. Tuberc.* **57**:528-533, 1948.
55. Tollen, W. B. Irregular discharge: problem of hospitalization of tuberculous. *Pub. Health Rep.* **63**:1441-1470, 1948.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

BENJAMIN CASTLEMAN, M.D., *Associate Editor*

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CASE 35121

PRESENTATION OF CASE

First admission. A thirty-two-year-old woman entered the hospital for treatment of an old knee injury sustained two and a half years previously, when she severely bumped and twisted the left knee in a fall from a stepladder.

The initial pain and swelling subsided within a few weeks, and she was able to walk about fairly well despite some aching pain, stiffness and slight weakness, which persisted for about one year. Nine months before entry she again severely wrenched the left knee while running and subsequently suffered pain and stiffness on walking. Occasionally the knee gave way under her, although it never really locked. She consulted a doctor, who noted bulging and tenderness of the medial side of the left knee joint. X-ray films were reported as normal. An operation was performed, with removal of a torn medial meniscus. Following operation the knee continued to be painful, and she was unable to extend it completely, despite physiotherapy. Approximately five months later the knee was re-explored, and a loose body removed. This failed to bring any improvement, and the stiffness, failure of extension and aching pain continued.

The past history was noncontributory except for congenital syphilis manifested by interstitial keratitis of the right eye, which was intensively treated by arsenicals, bismuth and penicillin. The blood Wassermann reaction continued to be positive despite therapy.

Physical examination showed a well developed and well nourished woman. There was interstitial keratitis of the right eye, but the pupils reacted to light and accommodation. The left knee was held in 20° permanent flexion, with a flexion swing of 60°. There was considerable tenderness on palpation of the joint, most marked laterally.

The temperature was 98°F., the pulse 70, and the respirations 20. The blood pressure was 135 systolic, 80 diastolic.

Examination of the blood disclosed a white-cell count of 8100, with 81 per cent neutrophils. Both the blood Wassermann and Hinton tests were positive. X-ray films of the left knee showed that the joint surface was smooth, but the space was narrowed, and there was marked thickening of the soft tissues of the joint space. There was no bone destruction (Fig. 1 and 2). The right knee showed no definite abnormality. A tuberculin test in a dilution of 1:100, 000 was negative.

The knee was manipulated under anesthesia and brought to as much extension as possible, but there remained 20 to 25° fixed flexion. Following this the temperature spiked daily to 100 and 101°F. for about five days. She then became afebrile and on exercise function improved considerably so that she was able to flex the knee 80° and lacked only 5° of full extension.

Second admission (two months later). Following discharge the patient was able to walk with crutches and to continue her exercises. She still had diffuse soreness on walking and at times suffered from a burning pain over the medial aspect of the joint, even at rest. Use of the knee definitely aggravated the pain and swelling of the knee.

Physical examination was unchanged except for considerable increase in the swelling and thickness of the periarticular tissues of the left knee posteriorly as well as to each side. There was diffuse tenderness and increased warmth.

Laboratory studies showed normal urine and blood counts. The sedimentation rate was 36 mm. in one hour.

On the second hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. WILLIAM S. CLARK: This record represents a common problem in the differential diagnosis of

monoarticular joint disease. The basic phenomenon responsible for the symptoms and signs described here may range all the way from reversible, poorly understood inflammatory processes of the synovial tissues to highly malignant and rapidly fatal tumors. Adequate clinical information and sound clinical hypothesis are particularly important because it is sometimes difficult to obtain adequate tissue for examination from various joints for anatomic reasons. We assume that in taking this history particular attention was paid to the possibility of involvement of other joints. Usually, in taking a history, we ask the patient indirect questions, inquiring about arch supports, lumbago or sciatica, and in this manner we frequently find that the presumed monoarticular disease is a part of a generalized type of joint involvement. However, on the basis of the information we have been given, we will start with the assumption that this process was localized in one joint. It is also noted that there were no constitutional manifestations such as fatigue, weight loss or fever to indicate that this monoarticular joint involvement was related to a systemic disease such as rheumatoid arthritis or a chronic infectious process. We can therefore focus most of our attention on the findings in the knee. The original symptoms followed an injury. This is a common story in joint involvement, regardless of the underlying process. A meniscus was removed at a previous operation, but there is no information concerning the pathology at that time. I am particularly interested in knowing if the synovial fluid was hemorrhagic or not at that time. That operation apparently did not result in much improvement.

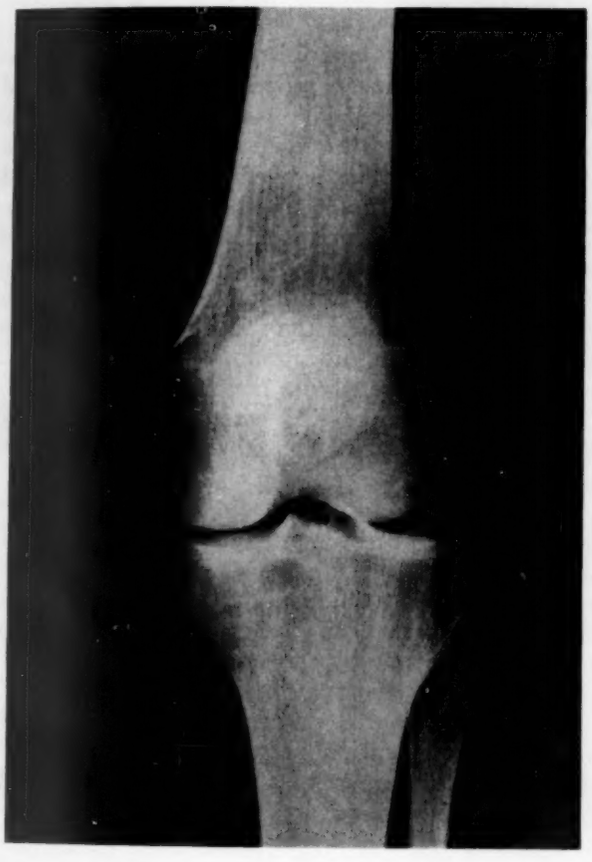

FIGURE 1.

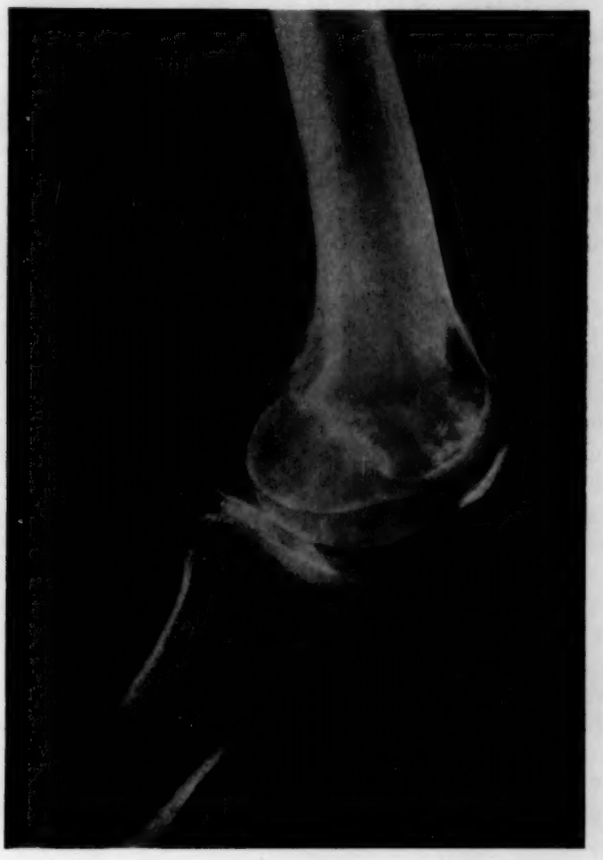

FIGURE 2.

As far as the laboratory work is concerned, two facts may be significant. The sedimentation rate was elevated, and the blood Hinton test was positive. A negative tuberculin test in a dilution of 1:100,000 is not significant because joint tuberculosis can be present with a negative test using even higher concentrations.

May we see the x-ray films?

DR. STANLEY M. WYMAN: We have a single set of films taken of both knees, and they show the prominence of soft-tissue shadows adjacent to the left knee, particularly on the medial aspect and, to a lesser extent, laterally. This is well seen extending posteriorly to the joint. I believe the nature of the soft tissue is more consistent with a

mass than with fluid in the joint space or simply thickening associated with infection. The cortical surfaces of the left knee appear preserved, but there is extensive osteoporosis in the femur and in the tibia particularly on the femoral side in the region of the condyles. There are tiny areas of increased density within the soft-tissue mass, which suggests flecks of calcification.

DR. CLARK: There are a number of lesions that might be considered. In spite of the absence of constitutional manifestations, we must consider the possibility of monoarticular rheumatoid arthritis. It is difficult to make such a diagnosis during a small segment of the course of the illness. Usually, such a conclusion is based on following the patient for a period and by eventually ruling out other possibilities. The anteroposterior x-ray film reveals changes in the bones consistent with that diagnosis. However, the periarticular thickening is more than one would expect in rheumatoid arthritis, in spite of the fact that synovial tissue proliferation is a basic part of its pathology. Furthermore, the subchondral destruction in the lateral view is more complete and more localized than we usually see in rheumatoid arthritis. Tuberculosis of the knee must be considered in this differential diagnosis. The x-ray films do not suggest an infectious process, and tuberculosis is not indicated by systemic manifestations. The marked soft-tissue swelling is against that diagnosis. Syphilis must be mentioned. Almost every form of joint disease has been attributed to this infection. I suspect that much of the syphilitic arthritis reported in the literature is actually related to rheumatoid arthritis. Gummas of the joint do occur, and they are in almost all cases related to bone. In my experience, the 2 proved cases of syphilitic involvement of the knee have been gummas of the patella. The problem of Clutton's joints (arthritis associated with congenital syphilis) need not be considered in spite of the presence of apparently healed interstitial keratitis. The fourth diagnosis we have to consider is tumor. I give greater weight to this possibility after seeing the great amount of thickening in the x-ray films. There are two types one might encounter in joints. The first is the benign giant-cell tumor of synovia, usually referred to now as pigmented villonodular synovitis. For those not familiar with this terminology, in relation to benign synovial tumors, I would like to give a word of explanation. Pigmented villonodular synovitis is a term applied by Jaffe[1] to the yellowish-brown, tumor-like lesion of the synovial membrane reported in the literature since 1865. This lesion has also been called benign giant-cell tumor of the synovial membrane, xanthoma, xanthogranuloma, xanthomatous giant-cell tumor and myeloplaxoma. Its morphology is well known to pathologists. We have recently analyzed 10 such cases here. The patients were of both sexes. The ages ranged between seventeen and eighty years. The duration of symptoms had been from a few hours to fifteen years. There was monoarticular involvement in all cases, with a knee involved in 70 per cent. The patients usually complained of recurrent joint pain. X-ray changes were present in 30 per cent. The characteristic finding was bloody synovial fluid with counts ranging from 28,000 to 2,000,000 red blood cells per cubic millimeter.

The second type of tumor is the synovioma or synovial-cell sarcoma. This is not a common tumor, and I have had very little experience with it. I have drawn chiefly on the literature for information.[2] The synovioma can produce this picture with these symptoms. I am not so certain about the x-ray findings of bone destruction. The synovioma is not ordinarily confined to the joint cavity, and may extend beyond the joint into adjacent structures.

I had the original impression that this knee involvement was either monoarticular rheumatoid arthritis or pigmented villonodular synovitis. Since seeing the x-ray films I favor tumor and would place benign giant-cell tumor of the synovia or pigmented villonodular synovitis as the more likely diagnosis.

DR. WYMAN: I think the description as given by Dr. Clark is most compatible with the x-ray findings — namely, a tumor. It has been my experience and that of others that this suggestion of fine calcification is not uncommon with synovioma. As to whether there is true bone destruction at all, it seems to me more like osteoporosis — atrophy of disuse. Therefore, I should consider synovioma primarily.

DR. CLARK: I probably did not pay enough attention to the presence of flecks of calcium. I do not know whether there is actual osteoporosis in pigmented villonodular synovitis. I think Dr. Castleman has seen one case with some involvement of the marrow by the tumor.

DR. BENJAMIN CASTLEMAN: Yes.

DR. CLARK: We have been inclined to assume that the decalcification in pigmented villonodular synovitis is analogous to the decalcification that occurs in hemophiliac arthritis. I would like to explain its symptoms by repeated joint apoplexies. Whether the atrophy comes from disuse or an autonomic phenomenon, we do not know. I agree that this does not appear to be the decalcification of something eroding into the bone or eroding within the bone.

DR. MARIAN ROPES: Essentially I used the same type of reasoning as Dr. Clark. I first thought of tuberculosis and rheumatoid arthritis. I tended at that time to rule out tumors on the fact that the patient had had two operations. Later, when we found that biopsy had not been done at either operation, a thing that occurs too commonly in opening a joint, I considered villonodular synovitis the most

likely diagnosis. Again, I ruled out malignant tumor, partly on the duration of the course.

Clinical Diagnoses

Traumatic synovitis.
Villonodular synovitis?

Dr. Clark's Diagnosis

Pigmented villonodular synovitis (benign giant-cell tumor of synovia).

Anatomical Diagnoses

Synovioma of left knee, with metastases to vertebras, clavicle, ribs, pelvic bones, peritoneum, abdominal lymph nodes, lungs and liver.
Compression myelitis, twelfth dorsal vertebra.
Decubitus ulcer, sacral region.
Cystitis, acute and chronic, severe.
Bronchopneumonia.
Interstitial keratitis.

Pathological Discussion

Dr. Tracy B. Mallory: This knee was explored by Dr. Edwin F. Cave, who found a marked thickening with papillary excrescence of the synovial membrane. Some of the nodular excrescences showed a brownish, chocolate-colored staining, rather suggestive of villonodular synovitis. Microscopical sections, however, did not look like that, and we were inclined to think that we were dealing with malignant neoplasm, although it did not look like any synovioma that we had seen, and we were unable to name it. We sent the slides to Dr. Jaffe, who said he did not know what it was and thought that it was probably a granulomatous lesion, although he could not rule out malignant tumor. We also sent them to Dr. Granville Bennett, who said that he thought it was tumor but did not know what kind of tumor.

The patient at that time refused amputation and was permitted to go home after partial excision and fusion of the knee joint. Pain continued and became so severe that she returned a couple of months later and consented to amputation. At that time very extensive neoplastic involvement of the remnant of the knee joint was found. Once again she was allowed to go home, and a few months later developed evidence of metastases in the lower spine, with transverse myelitis. She finally died of complications of the myelitis. At autopsy we found metastatic lesions in the bones, including the ribs and several vertebras. There was one minute nodule in the lung, one in the liver and many serosal implants throughout the peritoneal cavity, one of which had invaded the ovary, and a great many retroperitoneal nodes were involved. The distribution of the metastases was a most unusual one for any form of tumor. The metastases are no easier to classify than the primary tumor. Synoviomas, as I have seen them, surprisingly rarely show very much fibrous tissue, and yet this tumor was, in places, quite scirrhous. Characteristically, they show two types of cells, one of which appears epithelial; the other is spindle-shaped and suggests primitive mesenchyme. There are often clefts in the tumor that appear to be lined with the epithelial elements. I could find no such areas in this case. A rather noticeable feature about this tumor was that many of the cells were coarsely vacuolated. We thought briefly of liposarcoma, but fat stains were negative. Some glycogen was demonstrated in the vacuoles. Neither the character of the cells nor the general architecture of the tumor corresponds to what is ordinarily seen in synovioma. Yet the primary location of the tumor in the synovia of a knee joint is characteristic. I think synovioma is the diagnosis we have to make, despite the rather atypical histologic appearance. Our experience with synoviomas is that they have all been very highly malignant, and early metastases have been the rule.

There was one very interesting phenomenon, which I have never noted before. On the edge of the metastases in the liver and lung the neighboring parenchymal epithelial cells had been stimulated to marked growth. In the lung, for instance, the neighboring alveoli showed a lining of high columnar epithelial-like pulmonary epitheliomatosis. In the liver there was marked proliferation of bile-duct epithelium all around the metastasis as if some growth-stimulating substance were being excreted by the tumor. The fact that this phenomenon was seen in two different organs, each time in close approximation to a metastatic nodule, makes me believe that it was not coincidence. I think there must have been some such peculiar growth stimulation associated with this tumor.

A Physician: If a biopsy had been taken at the first operation, it would have helped the treatment, would it not?

Dr. Mallory: If the diagnosis could have been made on the original operation, which I think is doubtful in view of the fact that several months later three pathologists disagreed on the diagnosis, immediate amputation might have made a difference. Some six months was lost in this case.

Dr. Clark: Most people ignore their lame knees until a diagnosis is of very little help if it turns out to be a malignant tumor.

References

1. Jaffe, H. L., Lichtenstein, L., and Sutro, C. J. Pigmented villonodular synovitis, bursitis and tenosynovitis. *Arch. Path.* **31**:731-765, 1941.
2. Bennett, G. A. Malignant neoplasms originating in synovial tissues (synoviomata). *J. Bone & Joint Surg.* **29**:259-291, 1947.

CASE 35122

Presentation of Case

A thirty-eight-year-old man was admitted to the hospital complaining of cramps, diarrhea and weight loss.

The patient was in good health until one month before admission, when crampy, right-lower-quadrant pain, accompanied by right-lower-quadrant distention, appeared. This was occasionally associated with vague, left-upper-quadrant epigastric distress. The episodes were intermittent and occurred at any time of the day or night and were sufficiently severe to prevent sleep. There was no relation to eating. Some relief was obtained from belching or bowel movements. Until the onset of the illness he had been chronically constipated. A month before admission the bowel movements became loose and watery, and he had five or six diarrheal stools daily, which contained a few flecks of bright-red blood without pus or mucus. These symptoms lasted for five days and then disappeared for two weeks, when they recurred and gradually became more severe. The appetite diminished. On the night before admission he vomited for the first time. During the past year his weight went from 135 to 118 pounds because he did not have enough to eat.

His father was living, aged seventy-five, and had been operated upon eight years previously for "cancer of the stomach." A brother had been operated on for "cancer of the rectum" several years previously.

Physical examination showed an undernourished, underdeveloped man. The abdomen was moderately distended, and the lower half was tympanitic, more on the right than the left. The peristaltic sounds were normal. There was considerable direct and rebound tenderness in the right lower quadrant, with voluntary spasm. No mass was felt. There was mild bilateral costovertebral-angle tenderness. The left testicle was undescended, and a partially reducible left direct inguinal hernia was present. On rectal examination hemorrhoids were found, and there was marked tenderness in the right vault, but no mass was felt.

The pulse was 88, and the respirations 20. The blood pressure was 120 systolic, 80 diastolic.

Laboratory examination demonstrated a normal urine. The white-cell count was 8800, with 88 per cent neutrophils. The hemoglobin was 12 gm. The stools were liquid, brown and guaiac positive. The serum protein, prothrombin time and cholesterol were all within normal limits. X-ray study of the chest demonstrated no abnormality. In the abdomen a plain film suggested a mass in the right upper quadrant, partially outlined by gas within the colon. On barium enema the barium flowed to the midtransverse colon, where a complete obstruction was met. Barium flowed along the margins of a luminal mass for a short distance. There was a large palpable mass in this area. A sigmoidoscopic examination showed no abnormalities, but "the bowel seemed a bit spastic."

On the second hospital day a mass was felt to the right and below the umbilicus. On the following day it had moved to the left half of the abdomen to the level of the umbilicus.

An operation was performed five days after admission.

Differential Diagnosis

Dr. W. Philip Giddings: The salient points of this history are that the patient was a man of thirty-eight years whose symptoms were of one month's duration. There appear to have been two different sets of symptoms, both referable to the lower gastrointestinal tract. The first consisted of intermittent diarrhea with five or six loose stools daily and with small amounts of bright blood in the stools. The second comprised episodes of right-lower-quadrant pain of significant severity, accompanied by right-lower-quadrant distention, partially relieved by eructation or defecation and apparently attended by vomiting the night before admission.

There was a suggestive family history of gastrointestinal cancer. Physical findings directed attention to the right lower quadrant and were compatible with ileus. Under observation there was a palpable mass in the right lower quadrant, which twenty-four hours later had moved to the left side. Proctoscopy was negative, and the presence of blood in the stools was confirmed. Blood chemical findings were normal. The polymorphonuclear leukocytosis suggested an inflammatory component to the disease, but we do not know whether or not there was fever.

The finding of hernia and cryptorchidism on the left raises the question whether or not either might have been related to the present illness. However, the reducibility of the hernia rules it out as a source of trouble, and the likelihood that a tumor in an undescended left testis would cause primarily right-sided bowel symptoms seems small. I believe these conditions were not related to the present illness.

The barium-enema films are revealing. There was a convex defect in the midtransverse colon, with the margins of an obstructing, fairly smooth, intraluminal mass clearly outlined. This appearance was the reverse of the concavity with "shelf" formation commonly seen in carcinoma of the colon. It is, however, characteristic of intussusception.

In addition to the x-ray appearance, there are three reasons for believing that this man suffered from intussusception. The first is the recurrent nature of the acute episodes, with intervals of relief, suggesting repeated bouts of a process that relieved itself.

The second is the observed migration of a mass from the right to the left side of the abdomen, which

in such a case as this may be regarded as practically pathognomonic. And the third is the fact that an apparently satisfactory barium enema was repeated on the following day. This suggests that the Surgical Service was anxious to learn whether spontaneous reduction had occurred or possibly that they hoped to be able to reduce the intussusception by hydrostatic pressure. From the appearance of the films I judge that reduction did not occur.

We must now consider the causes of intussusception in adults. The acute, spontaneous condition observed in children is very rarely, if ever, seen in adults. Furthermore, the recurrent nature of this man's complaint, as well as the presence of diarrhea with blood persisting between the acute episodes, makes me believe that there was some underlying, intrinsic lesion in the bowel that precipitated the intussusception.

Apparently the commonest cause of this condition is submucous lipoma of the colon.* Bloody diarrhea can occur in this condition if there is ulceration of the mucosa overlying the tumor. Benign polyps of the colon have been described as the precipitating factor in intussusception in adults. Carcinoid of the ileocecal region has also, I believe, been described in this relation. I see no reason why any benign tumor of the colon, or possibly of the terminal ileum, might not have been at the root of this man's trouble. The same statement may be made of Meckel's diverticulum. However, I do not see how we can arrive at a positive conclusion concerning just what the lesion was.

On a statistical basis I shall say that submucous lipoma of the cecum or ascending colon is the most likely diagnosis, with mucosal ulceration and intussusception.

Dr. F. Thomas Gephart: This patient's history suggested regional ileitis. When the Surgical Service first saw the patient he had developed this large, midepigastric mass and had the barium-enema findings of intussusception. It seemed unusual to see such a large mass result solely from intussusception without more marked signs of acute intestinal obstruction. This was one point in favor of the diagnosis of carcinoma of the transverse colon. We realized the patient might well have an intussusception, but since he had no signs of acute obstruction, we decided to prepare him for bowel surgery for two days with antibiotics, start a Miller–Abbott tube and transfuse him, watching carefully for signs of obstruction.

After induction with ether anesthesia the large, midepigastric mass had disappeared, and a small firm mass could be felt in the right lower quadrant. At operation the intussusception was found to be reduced, and a hard, doughnut-shaped tumor was found involving the cecum near the ileocecal valve. Though the tumor completely surrounded the bowel, the lumen was not obstructed.

Clinical Diagnosis

Carcinoma of the colon, with intussusception?

Dr. Giddings's Diagnosis

Submucous lipoma of cecum, with intussusception.

Anatomical Diagnosis

Adenocarcinoma of cecum, with previous intussusception.

Pathological Discussion

Dr. Benjamin Castleman: In the cecum surrounding the appendiceal orifice was an elevated, indurated and ulcerated circular tumor about 5.5 cm. in diameter. The appendiceal os protruded into the center of the tumor. The appendix itself was slightly thickened. Microscopically, the tumor was the usual adenocarcinoma, invading but not extending through the muscularis. The ileocecal valve was not involved, nor were any of the regional lymph nodes.

Usually when a carcinoma produces intussusception it is the polypoid type. I suppose in this case the slight involvement of the muscularis and perhaps the unusual location of the tumor contributed to the mobility of the bowel. The intussusception must have included the appendix.

*Pack, G. T., and Booher, R. J. Intussuscepting submucous lipoma of right colon. *Surg. Clin. North America* **27**:361-372, 1947.

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GREATER BOSTON COMMUNITY SURVEY

IT HAS been apparent for some time that the per-capita expenditure for charitable purposes in Greater Boston has been more generous than in a number of comparable areas. It has not been so apparent that the returns from each of the multiplicity of agencies involved has always been on a commensurate scale. A multiplicity of competitive appeals has developed, moreover, each of which makes its demands upon the public conscience and the public purse. When the dollars themselves, in addition to shrinking in value, began to shrink in numbers, it seemed obvious to certain persons interested in the Greater Boston Community Fund and the Greater Boston Community Council that something should be done about it.

Accordingly, Robert Cutler, well known for his interest in the public welfare, was invited early in 1947 to form a committee of citizens to investigate the problem. This committee of 180 persons met in March, two years ago, to launch the enterprise. The result was the Greater Boston Community Survey of the more than 800 voluntary and tax-supported agencies in 55 of the independent communities that make up the nonpolitical and vaguely defined area known as Greater Boston.

The basic object of the Survey has been "to make sure that the charitable dollar annually raised in Greater Boston does the greatest good for the greatest number in the most economical, effective way." It has been carried on and its results finally approved by an executive committee of 16 members, who, at the beginning of their labors, selected Robert P. Lane, of New York, as director of the Survey. The report of the Survey has been accepted by the Committee of Citizens.

The task has been difficult and many of its problems unprecedented. As the director stated in his foreword to the final summary report, recently issued:

> In the cities and towns of Greater Boston are found some of the country's oldest voluntary agencies, a few of them with some of the country's largest capital reserves; agencies established and for decades supported by persons bearing names that are honored throughout the country. Here are agencies that march in the forefront of advancing professional practice. Here are agencies that were once distinguished pioneers in important fields, still unforgetful of their early glory. Here are some of the newest and some of the oldest methods, and certainly some of the most tenacious traditions, in American public welfare and public health. Here in these independent, self-governing communities, are found a local pride, a resistance to outside control, a determination to manage one's own affairs, that are the very pith of the American spirit. Tax-supported and voluntary alike, the social and health agencies of Greater Boston present both an unparalleled opportunity and an unparalleled challenge to any group of lay citizens and professional workers who undertake a survey of this ancient, complex and justly proud community.

The director further stated two "preconceptions" that might be accepted as basic principles wherever the activities and the support of any social agency are scrutinized. The first is that all agencies, regardless of their auspices and the source of their funds, are engaged on a common task for the benefit of all

the people. The second is that governmental agencies must acknowledge and discharge their statutory obligations and that, in the instances covered by the present study, the communities of Greater Boston should accept all the financial aid that federal and state laws make possible.

The fiscal troubles in which the social and health services of the area find themselves are due to a variety of causes; and a variety of remedies, some of them drastic, are necessary to correct them. The failure mentioned above of governmental agencies, "charged with the legal duty to render certain services to people who meet clearly stated conditions," is an important cause, and it is appropriate to note that Greater Boston has received a smaller percentage of help from federal sources than the other areas with which it was compared — 9.4 per cent against an average of 11.8 per cent. Voluntary agencies should not use voluntary funds to pay for such services.

As corollaries to this principle, it should be established that when the provision of certain services has become widely accepted as a proper duty of government, it is mistaken community policy to support such services indefinitely from limited voluntary contributions, and that tax-supported agencies obtaining service from voluntary agencies should fully reimburse those agencies for the services received.

Needless duplication and overlapping of services, as they now exist, should be done away with; agencies should combine in some instances and should transfer their functions to competitive agencies and go out of business in others. Some services now supported by voluntary community funds should become self-supporting.

The Survey finally recommends that at the highest level a strong central agency should be established for fund raising, planning and budgeting, to replace its excellent but less adequate parents, the Greater Boston Community Fund and the Greater Boston Community Council.

In an area where "some of the newest and some of the oldest methods, and certainly some of the most tenacious traditions, in American public welfare and public health" exist, among more than 800 agencies, reforms may be difficult to institute. The very number of agencies involved, however, indicates the inefficiencies that must be remedied. The writing on the wall is in red ink and is preceded by a dollar sign.

DISREGARDED SEEDBED OF THE TUBERCLE BACILLUS

For adequate control or eradication of a disease like tuberculosis it is essential to know the sources of the infection and how it is spread from those sources. The steady decline in mortality figures is usually interpreted as indicating that the sources of infection are becoming fewer and that the disease is becoming of minor importance. Studies in certain limited population groups, however, have indicated that incidence and mortality are actually independent of each other and that the amount of clinically active tuberculosis is the result of these two. Only a small proportion of attempts to determine the "source case" for any new patient with tuberculosis are successful, and this must mean that the majority of new cases arise from clinically unimportant or clinically unrecognized sources.

Medlar and his co-workers* attempted to discover some of the unrecognized sources through a careful study and analysis of the autopsy material from Bellevue Hospital. The large and varied clinical and autopsy material seen at that hospital offered an excellent opportunity to determine on the one hand the incidence of deaths from tuberculosis and on the other the incidence of unhealed tuberculosis in persons who died from other diseases. They analyzed the post-mortem data of all patients over fifteen years of age for the ten-year period, 1935-1944, in relation to age, sex, race, the presence or absence of caseous foci or cavities in the lungs, generalized miliary tuberculosis and tuberculosis as a primary cause of death or as an incidental finding in persons who died of other diseases and the clinical diagnosis in relation to the recognition of the tuberculosis that was found at autopsy. They looked particularly for caseous foci in the lungs, as indicated by areas of necrotic tuberculous pneumonitis, which, when they soften and are extruded, serve as a source from which tubercle bacilli may be

*Medlar, E. M., Spain, D. M., and Holliday, R. W. Disregarded seedbed of tubercle bacillus. *Arch. Int. Med.* 81:501-517, 1948.

scattered within the lung and to the outside world. Since the results of this analysis are most revealing, some of the highlights are summarized.

With respect to race they found that in most cases in which tuberculosis was recorded in the autopsy records of Negroes it was the primary cause of death, whereas 29 per cent of white patients died from diseases other than tuberculosis. This suggests that if progressive tuberculosis becomes established in Negroes, they seldom survive long enough to die of other causes, whereas white persons often do. For that reason caseous foci were often mentioned as incidental findings in white patients.

With respect to age, it was found that tuberculosis was the cause of death in all patients under thirty years in whom unhealed tuberculous lesions were recognized, but the disease was the cause of death in only half the patients over seventy years old. Tuberculosis was diagnosed clinically in 89 per cent of the cases in which it was the primary cause of death. This varied with the age, however, for it was diagnosed in about 97 per cent of those under thirty years of age and in only 60 per cent of those over seventy years. Even in cases of tuberculous cavities in the lungs the diagnosis was made in only 70 per cent of the patients over seventy years of age. There was a general decrease in the clinical diagnosis of tuberculosis with the increase of the age of the patient.

It was also evident from these data that unhealed tuberculosis received little clinical attention in persons who died from other diseases. The clinical diagnosis of tuberculosis was recorded in less than half such patients with tuberculous cavities in the lungs.

The Bellevue pathologists also compared their autopsy data with the mortality figures for the same period for persons over fifteen years of age throughout the City of New York. The hospital material contained a somewhat lower proportion of persons over seventy years old. Proved tuberculous deaths in all ages were twice as frequent in the autopsy series as in the City series. The ratio between the Bellevue figures and those from the City was 1.4:1 for patients under thirty years and 3.9:1 for those over seventy years. About three fourths of the autopsied cases from Bellevue Hospital in patients under sixty years of age who died from tuberculosis were from the special service for the treatment of diseases of the chest, whereas in the group over seventy years of age, more than two thirds of the cases were from other services. It therefore seems that the higher proportion of deaths from tuberculosis at Bellevue was not due solely to the fact that there is a large active service for chest cases in that hospital.

Another interesting observation emerged from a comparison of incidence of unhealed tuberculosis among autopsies in two periods — namely, from 1920-1922 and from 1940-1942. Since the mortality figures from tuberculosis declined markedly in this interval, it was expected that the incidence of unhealed tuberculosis in the autopsy material would show a corresponding decline. The data, however, showed little change in incidence of unhealed tuberculosis, but instead there was a shift in the age distribution of these lesions, there being proportionally fewer cases under fifty years of age in the latter period. This tends, of course, to reflect the trend in the aging in the population.

A comparison of two samples of data from the same generation — that is, those who were fifteen to twenty-nine years old in 1920-1922 and those who were thirty to forty-nine years of age in 1940-1942 — revealed two points: as the generation aged, the ratio of deaths from other diseases to the deaths from tuberculosis increased; and, in patients with unhealed tuberculous lesions, there was a decrease in the ratio of deaths from tuberculosis to deaths from other causes. Thus, the greater incidence of unrecognized disease in old people must be considered not only the result of the holdover of patients who survived from the time when the mortality (and presumably the incidence in young people) was high but also due to new cases occurring in older age groups.

Confirmatory evidence for this conclusion is also quoted from experiences of the Metropolitan Life Insurance Company, where employees originally having negative x-ray examinations and tuberculin tests have been followed for a number of years. The average age when these persons began their employment was twenty years, and yet 63 per cent of them were found to have acquired the disease from one to

ten years later. Moreover, 10 per cent were employed for over fifteen years before acquiring tuberculosis. A history of contact with known cases was elicited in only about 10 per cent of these new cases. Medlar and his associates believe, on the basis of their autopsy experience, that these infections are new ones acquired in adult life rather than latent ones too minute to be detected earlier. This is a good illustration of increments of tuberculosis in an adult population that was as free from demonstrable tuberculosis as it is possible to determine from x-ray studies.

In discussing their observations, Medlar and his co-workers bring out the fact that today the majority of persons ill with tuberculosis are restored to a state of clinical well-being and many survive for years to die eventually from some other cause. Throughout their life many of these persons continue to shed tubercle bacilli and thus constitute one part of the seedbed of this disease.

Data are also quoted to show that tuberculosis is not too well controlled. About two thirds of the deaths from tuberculosis in a single year in New York City occurred outside any hospital, and another third took place within a month of admission to a hospital. A significant proportion of patients with active tuberculosis leave the hospitals against medical advice, and many patients are admitted to the hospital only for clinical relapse of the disease. Furthermore, about 1 in every 8 newly discovered cases first becomes known through death registrations, and about half the patients with tuberculosis are discharged from hospitals either improved or unimproved. All these facts also relate to that part of the seedbed which is known.

The fact that unhealed tuberculosis is seldom found in the autopsy records of adults under thirty years of age when death was due to other diseases suggests that, if unaltered in its course, progressive tuberculosis is a highly fatal disease in young adults. The finding of unhealed lesions in increasing numbers of persons dead from other diseases, in proportion to those dead from tuberculosis, indicates that a progressive infection acquired in later life tends to be less explosive. Tuberculosis is therefore less likely to be suspected in persons over fifty years of age. This constitutes the unknown part of the seedbed, which the autopsy data indicate contains approximately 1000 persons with cavity formation per 100,000 of the population.

According to these workers control of tuberculosis — that is, the decrease in the continuity of the disease — requires intelligent supervision of the seedbed to prevent the return to the soil of the factors that favor the tubercle bacilli. This means a planned follow-up study of all persons with unhealed disease, including those with x-ray shadows, regardless of whether their disease is considered active or inactive. In addition, an intensified search must be made for a cure, in a pathological as well as in a clinical sense, of those who have a progressive disease. "The seedbed must be eradicated if tuberculosis is to be eradicated."

AMORY PRIZE AWARDS

The American Academy of Arts and Sciences is the custodian of a substantial sum of money, the interest of which is available each seven years for the award of the Francis Amory Prize to one or more persons who in the preceding septennium have made notable contributions to the "treatment and cure of diseases and derangement of the human sexual generative organs in general, and more especially for the cure, prevention, or relief of the retention of urine, cystitis, prostatitis, etc." It was the expressed wish of the donor that the prize be awarded preferably for some "cunning contrivance or invention," but if such an invention was not forthcoming, other means to the desired end might be recognized.

The awards for the preceding septennium were conferred at a meeting on December 8, 1948, by the president of the Academy, Howard Mumford Jones, and Professor E. B. Wilson, chairman of the Amory Prize Committee. A cash prize of $3500 was presented to each of six distinguished investigators: Dr. Alexander B. Gutman, of New York City; Dr. Charles B. Huggins, of Chicago; Dr. Willem J. Kolff, of Kampen, Holland; Prof. Guy C. Marrian, of Edinburgh; Dr. George N. Papanicolaou, of New York City; and Dr. Selman A. Waksman, of New Brunswick, New Jersey.

In commenting on the work of these scientists, Dr. Huggins, who made the principal address of the occasion, emphasized the close similarity between scientists and artists: both are devoted to the creation of orderliness and the search for truth among a host of confusing details. Like other forms of art, science can be dull or elegant, but good science is capable of evoking the highest intellectual pleasure in its creator and his auditors. "Good science finds itself equally at home in an institute of the Arts as of the Sciences."

"Medical research differs from the purer but not necessarily more elegant branches of science in the peculiarity that human beings with illness are its essential reason for being." And despite the necessity for quiet and leisurely reflection for creative thought the investigation should always be mindful of the sick patient in the background.

Urology was set forth as one of the youngest of the developed medical specialties — one of the finest accomplishments of this age; there is now no urologic illness that cannot in some way be improved by therapy. "Within the past ten years the treatment of venereal disease — a tremendous problem — has been solved." Nevertheless, the genitourinary system is extremely vulnerable to disease — mostly infections and tumors, which at one time or another afflict more than half of all human beings; hence, much more research remains to be done.

Among the 1948 recipients of the Amory prize, Dr. Gutman is notable for the discovery of the usefulness of serum acid phosphatase determinations in the diagnosis and management of malignant prostatic neoplasms. Dr. Huggins's splendid work on the influence of several hormones on prostatic secretion and on the diagnosis and treatment of cancer of the prostate is of world-wide renown. Dr. Kolff, following up the work of Abel, Rowntree and Turner, of Johns Hopkins, has developed a practical "artificial kidney" for the treatment of acute uremia. Prof. Marrian shared in the Amory Awards because of his searching investigations of steroid hormones that affect the functions of the generative tract, leading to important diagnostic and therapeutic measures. Dr. Papanicolaou's work on exfoliative cytology is coming to be widely applied not only to the diagnosis of cancer in the organs of the genitourinary tract but also to malignant growths in the hollow organs generally. Dr. Waksman's discovery of streptomycin has been a major factor in the triumphs of current urologic therapy.

Dr. Huggins concluded his Amory address with the following stirring words.

> We are all impressed by the vigor and power of the human mind as demonstrated by the use of the scientific method. Science is not concerned with whether its products are constructive or destructive; its only proper interest is in establishing truth. The velocity of scientific development in this age is tremendous. In the field in which Francis Amory was interested, God only knows what the next septennium will bring forth, but I can guarantee that it will be good news for sick people, if we can survive the prescriptions of the politicians.

The Amory Committee will welcome nominations for Awards for suitable work done in the current septennium ending in November, 1955.

DISASTER IN CHILE

In November, 1948, the library of the medical school and the department of parasitology of the Chilean Public Health Service were burned to the ground in a great fire. The scientific equipment, museum specimens, slides, colonies of insects and books and periodicals were completely destroyed. The Department of Parasitology is seeking the cooperation of the scientific world in the task of rehabilitating its collections for the purposes of teaching and research. There is great need of parasitology specimens, mounted or unmounted, histologic sections and insects and arachnids. Medical literature on the subjects of parasitology, biology, public health in general, epidemiology, vital statistics, rural health and health education, including reprints, is urgently needed. A first-class periodical entitled the *Revista chilena de higiene y medicina preventiva* is published at Santiago. The address for the present is Departmento de parasitologia, Cassilla 9183, Santiago, Chile.

The Boston Medical Library, 8 Fenway, Boston 15, in view of the magnitude of this disaster, is prepared to receive literary material, if sent prepaid, and arrange for its transportation to Chile. To avoid duplication, lists of available material should be sent to the Library before shipment.

MASSACHUSETTS MEDICAL SOCIETY

PRINCIPLES AND PROPOSALS

The following principles were adopted on February 9, 1949, by the Committees on Medical Economics and Public Relations of the Massachusetts Medical Society for presentation at the meeting of the Planning Committee of the American Medical Association on February 12, 1949:

1. We believe that the health of the people served by prepayment insurance plans will be most benefited by medical care free of government administration and control.

2. We should like to call attention to the profligate waste and duplication in health programs operated by the government in regard to both hospital beds and personnel as reported by the Hoover Commission. We believe that compulsory health insurance operated by the Government would result in similar inefficiency.

3. We believe that the manner of expression of policy on the part of the American Medical Association has served to diminish public confidence in that body to the serious concern of many of the members of the association.

We believe that the policy of the American Medical Association should be one of more active and enthusiastic support of constructive proposals for more equitable distribution of medical care.

Therefore, we suggest as constructive proposals worthy of support the following:

1. The objective of adequate medical care in our free society is to make available to everyone — regardless of race, color, creed, financial status or place of residence — every known essential preventive, diagnostic and curative medical service of high quality. The attainment of such medical care must necessarily be an evolutionary process which will require the co-operation of all concerned over a period of years.

2. The principle of voluntary prepayment health insurance should be the basic method of financing medical care for the large majority of the American people; in order to remove the burden of unpredictable sickness costs and abolish the economic barrier to adequate medical services.

3. The success of any plan for medical care is dependent on the mutual co-operation of the public, those rendering professional services and the administrative agencies. This co-operation can be obtained only if those rendering the services are convinced that they will have a continuing authoritative voice in the formulation and execution of policies and plans, thereby assuming their proper share of responsibility.

4. Voluntary prepayment group health plans, embodying group practice and providing comprehensive service, when practicable, offer to their members excellent medical care. Hence such plans should be encouraged.

5. The people have the right to establish voluntary prepayment plans on any basis guarded by legal restrictions, necessary to assure proper standards and qualifications.

6. Provision of adequate medical care for those unable to obtain it by voluntary prepayment plans or by direct payment is the responsibility of the local or state government. Part of the burden of this responsibility may be assumed by charitable agencies. Federal grant-in-aid to state programs administered by state boards of health is an acceptable method of helping to meet this responsibility.

7. The medical care of those who are able to purchase it by voluntary prepayment plans or by direct payment is the responsibility of the individual.

8. The Federal Government should, wherever possible, support voluntary prepayment programs for hospital and medical care.

9. Eligibility for receiving benefits under a program aided by federal grants should be determined by the individual states or communities.

10. The patient shall have free choice of his physician, group of physicians, clinic or hospital from among those participating in any plan, provided that the physician, group of physicians, clinic or hospital shall have the right to refuse or accept the patient.

11. Physicians and other qualified persons rendering medical care shall receive adequate remuneration for their services.

12. The physician shall be free to elect or reject without prejudice participation in a medical care plan. The rights of the physician as to the choice of methods by which he is to be paid shall be fully protected.

13. We agree that the federal Government now should subsidize medical and nursing education, medical indigents, health and diagnostic centers, including mental, where not now adequate.

We believe effective organizations of state and district health councils would immeasurably improve the community concept of local health needs. The initiative of the people themselves, and especially of the medical and public health personnel, must provide the spark.

14. The Massachusetts Medical Society looks upon these basic principles as essential to the development of any successful medical-care plan, and as guides by which to evaluate medical-care plans that may be proposed in

the future, with the understanding that changing conditions may require their later revision.

We further urge that our delegates to the American Medical Association be instructed to press for the general adoption of the above principles and proposals by the American Medical Association.

H. QUIMBY GALLUPE, *Secretary*

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Tufts College Medical School, 1944.

HIRSCH, FRANK A., 64 Hampshire Street, Methuen.
Middlesex University School of Medicine, 1942. Sponsor: Dr. Rolf C. Norris, 247 Broadway, Methuen.

JOHNSON, LEONARD ALLAN, 7 Sheridan Street, Lawrence.
Middlesex University School of Medicine, 1943. Sponsor: Dr. Harold R. Kurth, 57 Jackson Street, Lawrence.

THOMSON, CHARLES RENFREW, 35 Hillside Avenue, Amesbury.
Dartmouth Medical School, 1943.

Harold R. Kurth, *Secretary*
57 Jackson Street, Lawrence

ESSEX SOUTH

BARTELS, CARL CRITTENDEN, 37 Oaklandvale Avenue, Saugus.
Northwestern University Medical School, 1944.

BERENSON, HILDA LANG, 349 Summer Street, Lynn.
Middlesex University School of Medicine, 1935. Sponsor: Dr. Joseph Lipton, 12 Kimball Road, Lynn.

BRODSKY, ERWIN, 376 Cabot Street, Beverly.
Middlesex University School of Medicine, 1942. Sponsor: Dr. Peer P. Johnson, 1 Monument Square, Beverly.

COLLINS, FRANK LAFORREST, JR., 12 Manning Street, Ipswich.
Tufts College Medical School, 1947.

FIELD, JOHN ALBERT, 625 West 169th Street, New York.
Columbia University College of Physicians and Surgeons, 1940.

FLYNN, NEWELL NEWMAN, JR., 3 Wadsworth Street, Danvers.
Tufts College Medical School, 1947.

MCINTIRE, FREDERIC JOSEPH, JR., 15 Elmwood Road, Marblehead.
New York University College of Medicine, 1943.

Henry D. Stebbins, *Secretary*
342 Essex Street, Salem

FRANKLIN

HOWARD, MALCOLM MCKAY, Greenfield.
Long Island College of Medicine, 1943.

THROPE, ROBERT STEPHEN, 64½ High Street, Greenfield.
Tufts College Medical School, 1947.

Milton M. Sisson, *Secretary*
31 Federal Street, Greenfield

HAMPDEN

ASHE, ALLAN MURRAY, 293 Elm Street, West Springfield.
College of Physicians and Surgeons, Boston, 1937. Sponsor: Dr. Frederick S. Hopkins, 146 Chestnut Street, Springfield.

BICK, MALCOLM WAGNER, 162 Pineywoods Avenue, Springfield.
Harvard Medical School, 1940.

BLAKER, SAMUEL IRVING, 262 Riverdale Street, West Springfield.
Middlesex University School of Medicine, 1926. Sponsor: Dr. John M. Birnie, 146 Chestnut Street, Springfield.

BRANCIFORTE, JOHN THEODORE, 123 Main Street, Bondsville.
Middlesex University School of Medicine, 1943. Sponsor: Dr. Joseph E. Slowick, 431 Main Street, Palmer.

FLAHERTY, JAMES R., 10 Squier Street, Palmer.
Tufts College Medical School, 1943.

GROSS, HAROLD ARNOLD, 38 Maple Street, Springfield.
New York University College of Medicine, 1946.

JOFFE, ELLIS, 235 Beech Street, Holyoke.
University of Brussels, School of Medicine, 1933. Sponsor: Dr. Patrick E. Gear, 188 Chestnut Street, Holyoke.

KANOWITZ, SIDNEY, 172 Dorset Street, Springfield.
Middlesex University School of Medicine, 1941. Sponsor: Dr. Alfonso A. Palermo, 121 Chestnut Street, Springfield.

KRAUS, EDWARD IGNATIUS, 397 Front Street, Chicopee.
Hahnemann Medical School and Hospital of Philadelphia, 1942.

LEVITZ, EDWARD ROBERT, 197 Beech Street, Holyoke.
Middlesex University School of Medicine, 1943. Sponsor: Dr. Adolph Franz, Jr., 276 Maple Street, Holyoke.

NATHANS, SYDNEY, 61 East Street, Chicopee Falls.
Kansas City University of Physicians and Surgeons, 1943. Sponsor: Dr. John M. Gilchrist, 121 Chestnut Street, Springfield.

PLATT, WARREN D., JR., 55 Mapledell Street, Springfield.
Columbia University College of Physicians and Surgeons, 1943.

ROGERS, ALEXANDER SIDNEY, 20 Brookline Avenue, Holyoke.
Middlesex University School of Medicine, 1943. Sponsor: Dr. Frederick W. Celce, 190 Chestnut Street, Holyoke.

ROSNER, ALFRED, 30 Center Street, Chicopee.
University of Vienna School of Medicine, 1943. Sponsor: Dr. Fred H. Allen, 16 Fairfield Avenue, Holyoke.

WILLIAMS, DAVID WILLARD, 312 Abbott Street, Springfield.
Harvard Medical School, 1943.

YETWIN, I. JACQUES, 84 Mayfair Avenue, Springfield.
Middlesex University School of Medicine, 1940. Sponsor: Dr. Frederick S. Hopkins, 146 Chestnut Street, Springfield.

ZIOLKOWSKI, HENRY JOHN, 170 Springfield Street, Chicopee.
Middlesex University School of Medicine, 1942. Sponsor: Dr. Eugene W. Beauchamp, 228 Springfield Street, Chicopee.

Walter W. Williams, *Secretary*
20 Magnolia Terrace, Springfield

MIDDLESEX EAST

ALFANO, LOUIS FRANCIS, 129 Lincoln Street, Melrose.
Tufts College Medical School, 1946.

HEATH, PARKER, 8 Fernway, Winchester.
University of Michigan Medical School, 1918.

MERRILL, JOHN PUTNAM, 11 Myrtle Street, Winchester.
Harvard Medical School, 1942.

Roy W. Layton, *Secretary*
8 Porter Street, Melrose

MIDDLESEX NORTH

BOUCHARD, GERMAIN JOSEPH, 54 Pentucket Avenue, Lowell.
Laval University Faculty of Medicine, 1943.

GREENSTEIN, SAMUEL SIDNEY, 42 South Walker Street, Lowell.
Middlesex University School of Medicine, 1943.

Brendan D. Leahey, *Secretary*
9 Central Street, Lowell

MIDDLESEX SOUTH

BELL, JOHN WILLIAM, 84 Duff Street, Watertown.
Northwestern University School of Medicine, 1946.

BIGELOW, FREDERICK SHATTUCK, Sudbury Road, Concord.
Harvard Medical School, 1942.

BRENNAN, ROBERT JOSEPH, 107 Eastern Avenue, Arlington.
Boston University School of Medicine, 1941.

CHERKAS, BENJAMIN, 1218 Massachusetts Avenue, Cambridge.
Middlesex University School of Medicine, 1937. Sponsor: Dr. J. Newton Newman, 140 Prospect Street, Cambridge.

CRANE, EMILY BROWNE TOWNSEND, 195 Marsh Street, Belmont.
Cornell University Medical College, 1945.

CRANLEY, JOHN JOSEPH, JR., 144 Winthrop Street, Medford.
Columbia University College of Physicians and Surgeons, 1944.

DONOVAN, JOHN HEAGERTY, 11 Windsor Terrace, Waltham.
Middlesex University School of Medicine, 1939. Sponsor: Dr. Joseph A. Holmes, 751 Main Street, Waltham.

DROSDIK, VINCENT A., 503 Main Street, Watertown.
Middlesex University School of Medicine, 1926. Sponsor: Dr. James J. Cammisa, 44 Leamington Road, Brighton.

FOLEY, ROBERT EMMETT, 77 Lyman Street, Waltham.
Cornell University Medical College, 1942.

FOSTER, AUGUSTA F., 420 Memorial Drive, Cambridge.
Tufts College Medical School, 1947.

GIANSIRACUSA, JOSEPH EDWARD, 17 Chandler Street, Belmont.
University of California Medical School, 1943.

GRIER, JAMES ROBERT STEWART, 57 MacArthur Road, Natick.
Harvard Medical School, 1941.

HANNA, GEORGE ALBERT, JR., 54 Newman Road, Malden.
Wayne University College of Medicine, 1942.

HUBBARD, EDWARD ORTON, JR., 131 Washington Street, Brighton.
Tufts College Medical School, 1940.

KAPLAN, SAMUEL, 38 Hyde Street, Newton Highlands.
Long Island College of Medicine, 1940.

KONEFAL, STANLEY HENRY, 29 Ashcroft Road, Medford.
Boston University School of Medicine, 1947.

LANE, MARVIN KENNETH, 181 Central Street, Holliston.
Middlesex University School of Medicine, 1943. Sponsor: Dr. Arthur Ward, Prospect Street, Framingham.

LAPPIN, SYDNEY HAROLD, 1999 Commonwealth Avenue, Brighton.
Middlesex University School of Medicine, 1935. Sponsor: Dr. David Ayman, 520 Beacon Street, Boston.

LYNCH, WILLIAM ALBERT, 10 Shaw Street, West Newton.
Tufts College Medical School, 1942.

METCALF, WILLIAM, 50 Irving Street, Newton Centre.
Johns Hopkins University School of Medicine, 1937.

MYERSON, RALPH MAYER, 525 Mystic Valley Parkway, Medford.
Tufts College Medical School, 1942.

NORMAN, PAUL PHENEAS, 300 Ferry Street, Malden.
Middlesex University School of Medicine, 1943. Sponsor: Dr. D. Joseph Duggan, 3 Hawthorne Street, Malden.

RICCI, ALPINE LOUIS, 807 Salem Street, Malden.
Middlesex University School of Medicine, 1937. Sponsor: Dr. D. Joseph Duggan, 3 Hawthorne Street, Malden.

ROBINS, ELI, 36 Highland Avenue, Cambridge.
Harvard Medical School, 1943.

ROSENTHAL, SAMUEL, 185 Hancock Street, Cambridge.
Middlesex University School of Medicine, 1937. Sponsor: Dr. John P. Nelligan, 2336 Massachusetts Avenue, Cambridge.

RUBINOW, MERRILL BENJAMIN, Cushing Veterans Administration Hospital, Framingham.
Long Island College of Medicine, 1942.

RUMERMAN, HERBERT, 131 Trapelo Road, Belmont.
Middlesex University School of Medicine, 1943. Sponsor: Dr. James Townsend, Mt. Auburn Hospital, Cambridge.

SEMENZA, NICHOLAS JAMES, 659 Moody Street, Waltham.
Middlesex University School of Medicine, 1942. Sponsor: Dr. Robert J. Cataldo, 820 Main Street, Waltham.

SILLIKER, STUART AUSTIN, 20 Highland Avenue, Cambridge.
Tufts College Medical School, 1945.

SOUZA, DOROTHEA LOUISE, 176 Harvard Street, Medford.
Tufts College Medical School, 1947.

STONE, ERIC PERCY, 894 Grove Street, Framingham.
Harvard Medical School, 1918.

VARVARO, EMMA MARIE, 114 Church Street, Waltham.
Middlesex University School of Medicine, 1936. Sponsor: Dr. Irving Fraim, 826 Main Street, Waltham.

WALES, BURTON LINCOLN, JR., 34 Irving Street, Cambridge.
Cornell University Medical College, 1944.

WEINBERGER, HOWARD J., 253 Waverley Street, Belmont.
University of California Medical School, 1941.

Alexander A. Levi, *Secretary*
481 Beacon Street, Boston

Norfolk

Ahern, John Francis, 14 Arcadia Street, Dorchester.
College of Physicians and Surgeons, Boston, 1913. Sponsor: Dr. John H. Cauley, 8 Carruth Street, Dorchester.

Barkin, Robert Ernest, 31a Englewood Avenue, Brookline.
Tufts College Medical School, 1942.

Bojar, Samuel, 32 Marshal Street, Brookline.
Johns Hopkins University School of Medicine, 1941.

Bookstein, Jacob, 322 Blue Hill Avenue, Roxbury.
College of Physicians and Surgeons, Boston, 1937. Sponsor: Dr. Saul M. Marcus, 520 Beacon Street, Boston.

Brodie, Sidney, 17 Stearns Road, Brookline.
George Washington University School of Medicine, 1943.

Chasen, Mignon Charney, Boston State Hospital, Dorchester.
University of Palermo, Italy, 1935. Sponsor: Dr. Walter E. Barton, 591 Morton Street, Dorchester.

DeLorme, Thomas Lanier, 12 Rustlewood Road, Milton.
New York University College of Medicine, 1943.

Dodge, George Augustus, II, 67 Griggs Road, Brookline.
Tufts College Medical School, 1941.

Etsten, Benjamin, 37 Gordon Road, Milton.
University of St. Andrews, Scotland, 1937. Sponsor: Dr. C. Stuart Welch, 30 Bennet Street, Boston.

Finck, Albert Jacob, 26 St. Paul Street, Brookline.
Harvard Medical School, 1941.

Garber, Jesse George, 26 Willow Crescent, Brookline.
Tufts College Medical School, 1941.

Golub, Benjamin Solomon, 90 Corbet Street, Dorchester.
Boston University School of Medicine, 1943.

Greene, Thomas Francis, 31 Roseland Street, Dorchester.
Tufts College Medical School, 1942.

Hazard, Sprague Whipple, 280 Independence Way, West Roxbury.
Columbia University College of Physicians and Surgeons, 1941.

Jansen, Alfred William, 33 Cedar Street, Norwood.
Tufts College Medical School, 1946.

Kaess, Kenneth Richard, 220 Aspinwall Avenue, Brookline.
Harvard Medical School, 1944.

Keiner, Samuel Sidney, 1763 Beacon Street, Brookline.
Middlesex University School of Medicine, 1936. Sponsor: Dr. Jacob Applebaum, 371 Commonwealth Avenue, Boston.

Kernan, Reginald Devereux, 138 Highland Street, Milton.
Harvard Medical School, 1944.

March, Herman Louis, 147 Ashmont Street, Dorchester.
Kansas City University of Physicians and Surgeons, 1935. Sponsor: Dr. David Davis, 416 Marlboro Street, Boston.

McGrath, Edward Francis, 27 Otis Street, Milton.
University of Pennsylvania School of Medicine, 1940.

Murray, Joseph E., 316 St. Paul Street, Brookline.
Harvard Medical School, 1943.

Ohler, Robert Loring, 6 Oakland Street, Wellesley Hills.
Harvard Medical School, 1941.

Ravin, Iver Solomon, 16 Short Street, Brookline.
Boston University School of Medicine, 1940.

Robinson, Charles, 56 Columbia Road, Dorchester.
College of Physicians and Surgeons, Boston, 1938. Sponsor: Dr. Hyman B. Goldberg, 2 Pasadena Road, Dorchester.

Slivkin, Stanley Edward, 2 Westmoreland Street, Dorchester.
Middlesex University School of Medicine, 1943. Sponsor: Dr. Saul Marcus, 520 Beacon Street, Boston.

Taggart, William James, 19 Abbott Road, Wellesley Hills.
Cornell University Medical College, 1944.

Tolnick, Bernard, 28 Ashcroft Street, Jamaica Plain.
Boston University School of Medicine, 1943.

Basil E. Barton, *Secretary*
10 Richwood Street, West Roxbury

Norfolk South

Kearns, Ralph Waldo, 53 Elm Avenue, Wollaston.
Kansas City University College of Physicians and Surgeons, 1942. Sponsor: Dr. Frederic N. Manley, 1200 Hancock Street, Quincy.

Nielsen, Odd Svennemann, 10 Valley Beach Avenue, Hull.
Boston University School of Medicine, 1947.

Readdy, Marjorie Elizabeth, 59 Pond Street, South Braintree.
Boston University School of Medicine, 1945.

Ebenezer K. Jenkins, *Secretary*
Norfolk County Hospital, South Braintree

Plymouth

Ambrosino, Joseph, 624 Main Street, Brockton.
Middlesex University School of Medicine, 1943. Sponsor: Dr. Alfred L. Duncombe, 167 Newbury Street, Brockton.

Berman, Carroll Zachary, 251 Belmont Street, Brockton.
Chicago Medical School, 1944. Sponsor: Dr. Albert R. Ferguson, Brockton Hospital, Brockton.

Blunt, James William, 583 Pleasant Street, Brockton.
Boston University School of Medicine, 1947.

DeFeo, Joseph Anthony, 109 Bedford Street, East Bridgewater.
Middlesex University School of Medicine, 1942. Sponsor: Dr. Alton Hurlburt, 81 Central Street, East Bridgewater.

Enos, Allen William, Broadway, Hanover.
Middlesex University School of Medicine, 1939. Sponsor: Dr. John C. Angley, Bryantville.

Foley, John J., Lakeville State Sanatorium, Middleboro.
Georgetown University School of Medicine, 1936.

Jacobson, Franklin Harold, 21 East Main Street, Avon.
Middlesex University School of Medicine, 1942. Sponsor: Dr. Saul C. Levine, 142 Main Street, Brockton.

Mason, Andrew Victor, 72 Spring Street, Bridgewater.
Tufts College Medical School, 1942.

McCluskey, John Edward, 932 Main Street, Brockton.
Middlesex University School of Medicine, 1940. Sponsor: Dr. M. F. Barrett, Main Street, Brockton.

Mulligan, John Joseph, 26 Summer Street, Bridgewater.
Middlesex University School of Medicine, 1942. Sponsor: Dr. Albert Hunt, School Street, Bridgewater.

Musante, Thomas Paul, 8 Laurel Street, Whitman.
Middlesex University School of Medicine, 1942. Sponsor: Dr. Thornton A. Landers, 572 Washington Street, Whitman.

Shaw, Elmer Ames, 43 Court Street, Plymouth.
Tufts College Medical School, 1940.

Verdon, Franklyn E., 76 South Street, Bridgewater.
Middlesex University School of Medicine, 1939. Sponsor: Dr. Frank E. Wheatley, Goddard Hospital, Brockton.

Zalon, Leo, 85 Broad Street, Bridgewater.
Middlesex University School of Medicine, 1931. Sponsor: Dr. William E. Hunt, 120 Main Street, Bridgewater.

Samuel Gale, *Secretary*
The Checkerton, Brockton

Suffolk

Denton, Jane Emerson, 9 Hancock Street, Boston.
Columbia University College of Physicians and Surgeons, 1945.

DiGiacomo, Charles, 501 East Broadway, South Boston.
Middlesex University School of Medicine, 1941. Sponsor: Dr. John J. Todd, 587 Beacon Street, Boston.

Evans, Richard Rice, 73 Gainsborough Street, Boston.
Albany Medical College, 1943.

Fahey, Robert John, 7 Webster Street, Winchester.
Tufts College Medical School, 1944.

Finlayson, Malcolm, Boston State Hospital, Dorchester.
Rush Medical College, 1942.

Finn, John Joseph, Jr., 30 Bennet Street, Boston.
Tufts College Medical School, 1941.

Freis, Edward David, 242 Shore Drive, Winthrop.
Columbia University College of Physicians and Surgeons, 1940.

Fulchino, Harry Louis, 13 Hancock Street, Revere.
Tufts College Medical School, 1944.

GRANDE, GAETANO GUY, 87 St. Andrew Road, East Boston.
Middlesex University School of Medicine, 1941. Sponsor: Dr. Charles J. Cataldo, 48 Byron Street, East Boston.

GRIESEMER, ROBERT DANIEL, Massachusetts General Hospital, Boston.
Harvard Medical School, 1943.

HACKWORTH, LORYE EDWARD, 25 Green Street, Waltham.
Harvard Medical School, 1943.

HINMAN, CRAWFORD H., 270 Brookline Avenue, Boston.
Harvard Medical School, 1941.

JEWETT, JOHN FIGGIS, 1 Anderson Place, Boston.
Harvard Medical School, 1938.

JILLSON, OTIS FIELD, 750 Harrison Avenue, Boston.
Tufts College Medical School, 1943.

KENNEY, JAMES FRANCIS, 74 E. Newton Street, Boston.
Boston University School of Medicine, 1945.

KILFOYLE, RICHARD MICHAEL, 84 Olney Street, Dorchester.
Tufts College Medical School, 1943.

KRAMER, PHILIP, 415 Commonwealth Avenue, Boston.
University of Chicago School of Medicine, 1939.

LICATA, DANIEL DAMIANO, 127 West Chestnut Street, Wakefield.
Middlesex University School of Medicine, 1937. Sponsor: Dr. A. Paul DerHagopian, 39 Cary Avenue, Chelsea.

MANFREDI, PHILIP L., 903 Beacon Street, Boston.
Midwest Medical College, 1934. Sponsor: Dr. Edward M. Hodgkins, 15 Bay State Road, Boston.

MCVEY, WILMA ANITA, 73 Gainsborough Street, Boston.
Albany Medical College, 1943.

OLSON, RAYMOND OSCAR, 195 Park Drive, Boston.
Harvard Medical School, 1942.

PAIGE, EMIL, 156 Pauline Street, Winthrop.
Tufts College Medical School, 1945.

PATTERSON, MARCEL, 20 Hemenway Street, Boston.
Tulane University of Louisiana School of Medicine, 1943.

PEPE, ENRICO ANTHONY, 160 Bennington Street, East Boston.
Harvard Medical School, 1943.

QUINBY, WILLIAM CARTER, JR., 88 Mt. Vernon Street, Boston.
Johns Hopkins University School of Medicine, 1940.

RIPA, ANTHONY SEBASTIAN, 735 Bennington Street, East Boston.
Middlesex University School of Medicine, 1936. Sponsor: Dr. Charles J. Cataldo, 48 Byron Street, East Boston.

ROE, BENSON BERTHEAU, 90A Myrtle Street, Boston.
Harvard Medical School, 1943.

SACCONE, WILLIAM A., 325 Malden Street, Revere.
Middlesex University School of Medicine, 1941. Sponsor: Dr. A. Paul DerHagopian, 39 Cary Avenue, Chelsea.

SACKS, MORRIS ISADORE, 45 Shirley Avenue, Revere.
Middlesex University School of Medicine, 1935. Sponsor: Dr. Arthur H. Vilker, 13 Nahant Avenue, Revere.

SHOUL, MELVIN IRVING, 33 Nobscot Road, Newton Centre.
Tufts College Medical School, 1947.

WEINSAFT, PAUL PINKAS, 238 Shore Drive, Winthrop.
University of Paris Faculty of Medicine, 1933. Sponsor: Dr. Maurice O. Belson, 199 Shore Drive, Winthrop.

WELLS, EDWARD BUIST, 80 Central Avenue, Newtonville.
University of Rochester School of Medicine, 1943.

WOLFSON, WILLIAM QUITMAN, 4349 South Ellis Avenue, Chicago, Illinois.
Middlesex University School of Medicine, 1943. Sponsor: Dr. Karl Singer, Michael Reese Hospital, Chicago, Illinois.

Charles G. Shedd, *Secretary*
422 Beacon Street, Boston

WORCESTER

ARENT, ANTHONY MICHAEL, St. Vincent's Hospital, Worcester.
Tufts College Medical School, 1942.

BIRD, LEE COULTHARD, State Hospital, North Grafton.
University of Wisconsin School of Medicine, 1933.

CAFARELLA, JOSEPH LEWIS, 21 Catalpa Street, Worcester.
Tufts College Medical School, 1944.

CROSS, JAMES EDWIN, 52 Newell Avenue, Southbridge.
University of Rochester School of Medicine, 1939.

CURRAN, JOHN FRANCIS, JR., 6 Westwood Drive, Worcester.
Tufts College Medical School, 1944.

DAVIS, LLOYD HAYES, 290 Main Street, Webster.
Northwestern University School of Medicine, 1922.

DIMATTEO, ANTHONY P., 11 Hartford Road, Worcester.
New York Medical College, Flower and Fifth Avenue Hospitals, 1934.

DISTEFANO, ANTHONY JAMES, JR., 296 Oak Street, Shrewsbury.
Marquette University School of Medicine, 1945.

JACOBS, NATHAN, 211 Main Street, Fisherville.
Middlesex University School of Medicine, 1934. Sponsor: Dr. Charles N. Church, Elm Street, Millbury.

JOHNSON, VERNER STANLEY, 41 Adin Street, Hopedale.
University of Nebraska, College of Medicine, 1947.

JONES, DAVID MANN, North Avenue, Mendon.
Tufts College Medical School, 1944.

KILROY, EDWARD FRANCIS, 644 Grove Street, Worcester.
Harvard Medical School, 1945.

KING, JOSEPH ANTHONY, JR., Worcester City Hospital, Worcester.
New York Medical College, Flower and Fifth Avenue Hospitals, 1947.

MCCREADY, FREDERICK JOSEPH, 68 Reed Street, Worcester.
Tufts College Medical School, 1943.

MCGOLDRICK, LOUIS GEORGE, 4 Suntaug Road, Worcester.
Tufts College Medical School, 1942.

MURPHY, JOSEPH FRANCIS, 29 Coes Street, Worcester.
Tufts College Medical School, 1942.

O'DONNELL, ANNE R., 36 Commodore Road, Worcester.
Tufts College Medical School, 1944.

SACHS, BARNEY EDWARD, 989 Main Street, Leicester.
College of Physicians and Surgeons, Boston, 1934. Sponsor: Dr. George R. Dunlop, 27 Elm Street, Worcester.

SHANNON, PAUL VINCENT, 159 Highland Street, Worcester.
Georgetown University School of Medicine, 1941.

WAKEFIELD, ROBERT DONALD, 777 Pleasant Street, Worcester.
University of Vermont College of Medicine, 1944.

WATERMAN, GEORGE ELWELL, Box 312, Clinton.
Boston University School of Medicine, 1946.

WITKOW, ALEXANDER, 32 Saxon Road, Worcester.
New York University College of Medicine, 1937.

Donald Hight, *Secretary*
27 Elm Street, Worcester

WORCESTER NORTH

BENTON, FRED WARREN, 30 Myrtle Avenue, Fitchburg.
Boston University School of Medicine, 1945.

GOLDMAN, ROBERT H., 65 Merriam Avenue, Leominster.
Kansas City University of Physicians and Surgeons, 1943. Sponsor: Dr. John J. Curley, 89 West Street, Leominster.

GOLDMAN, SIDNEY, 79 Prichard Street, Fitchburg.
Middlesex University School of Medicine, 1941. Sponsor: Dr. John J. Curley, 89 West Street, Leominster.

KIRSCHENBAUM, DAVID, East Gardner.
New York University College of Medicine, 1927.

ROSENBERG, JOSEPH, 918 Main Street, Fitchburg.
Middlesex University School of Medicine, 1943. Sponsor: Dr. Clarence N. McPeak, 18 Hartwell Street, Fitchburg.

RUBINO, BERNARD CHESTER, 145 Main Street, Athol.
University of Vermont College of Medicine, 1937.

James G. Simmons, *Secretary*
30 Myrtle Avenue, Fitchburg

DEATHS

BACON — Newton S. Bacon, M.D., of Cambridge, died on March 1. He was in his seventy-seventh year.

Dr. Bacon received his degree from Harvard Medical School in 1899. He was resident physician at Long Island Hospital and was a fellow of the American Medical Association.

A son and a brother survive.

HAND — Edward P. Hand, M.D., of Holyoke, died on January 4. He was in his sixtieth year.

Dr. Hand received his degree from Georgetown University School of Medicine in 1914. He was a former city physician, a member of the staffs of the Holyoke and Providence hospitals and fellow of the American College of Surgeons and American Medical Association.

Three brothers survive.

SKEIRIK — Jibran Y. Skeirik, M.D., of Lawrence, died on December 5. He was in his fifty-fourth year.

Dr. Skeirik received his degree from Harvard Medical School in 1929. He was a fellow of the American Medical Association.

His widow and a daughter survive.

BOSTON MEDICAL LIBRARY

REPORT OF THE PRESIDENT*

At this meeting I complete my term as your president, and it gives me considerable pleasure to present my third annual report on the state of the Library.

When I assumed office it did not take much study to realize that the first great need of the Library was more income. The budget did not balance, and we were drawing heavily on our invested funds, both restricted and unrestricted, to pay current bills. Consequently, economy was the rule, and while the Librarian and the Director did extraordinarily well with a very loyal staff, the service was not so good as might have been expected of a library of our size and reputation. There is, of course, a considerable value in a library building and its contents of books and periodicals, but its real value is in making these books and periodicals available to its members and to the public, in an attractive and prompt way. In other words, the value of a library may be measured in a sense by the circulation of its books and the use of its shelves. This, then, seemed the second objective, to increase the usefulness of the Library.

At the end of three years I am happy to say that the first of these objectives has been attained. When the dilemma in which the Library found itself was clearly presented to the members of the Massachusetts Medical Society, they saw that the Library was a very necessary part of medical education, that its collections should be available to all physicians and, therefore, that it ought to be considered a responsibility of the Society to help promote its efficiency and usefulness. Every fellow of the Massachusetts Medical Society is now a member of the Library, entitled to its privileges, sharing its responsibility (through its Society-appointed trustees) and contributing to its welfare. This is as it should be. Mr. Conant, speaking of the university library in his annual report, says, "neither teaching nor advanced scholarly studies in the humanities or the social sciences can go forward if a university library suffers from neglect" and I am sure that the same thing is true of medical science and its medical library.

Thanks to this splendid co-operation of the Massachusetts Medical Society the budget is now balanced for the first time in many years. We have paid back a considerable part of our indebtedness to our restricted funds, and with good luck we should be able to clean this up in a year or two at the most. This does not, by any means, put us on easy street. Money must still be saved or raised to complete the much-needed stacks.

Our extra income has enabled us to add several members to our staff, both housekeeping and technical. The extra housekeeping staff has enabled us to apply the mop and duster more efficiently and slowly to clean house. With our extra library staff we have been able to move and sort books that had accumulated in halls, closets and corridors. Some of these have been sold as duplicates, and some put in circulation, and several thousand volumes have been transferred to the Deposit Library on Soldiers Field. We now occupy about two thirds of the space we control in the Deposit Library. This service is rather expensive, but until we can complete the stacks there seems to be no alternative.

Among those added to our staff I might mention Mr. Charles Colby, who comes to us from the Army Medical Library with considerable training and experience in library work. For the present he will have charge of the Reference Room, with special assignments elsewhere as occasion demands and the Director thinks advisable.

I think I can also report considerable progress toward our second objective. In 1945 the use of the Library as measured by circulation was 31,298 volumes. In 1948 it was 53,515, a gain of 22,217 volumes in three years. If measured in terms of attendance the figures are not so dramatic, but even here there was a gain of nearly 3000. Furthermore, it is interesting to note that in 1947, the year before the membership included the fellows of the Massachusetts Medical Society, 9000 nonmembers availed themselves of the privilege of the Library in one way or another. We may therefore say not only that the financial structure of the Library is on a sound foundation but also that its usefulness to the medical profession has been made more available and comprehensive. I think it is fair to say that the smaller increase in attendance compared to the larger growth in circulation is due to the fact that our professional memberships have

*Presented at the annual meeting of the Boston Medical Library, March 1, 1949.

grown in numbers and that many more volumes are sent out to hospitals than heretofore. Instead of doctors coming to the Library for books, the books go to the doctor.

We have made some repairs, but more need to be done. The roof has been partially repaired only. There have been some painting jobs done, particularly in the office of the *Journal*, but more bright colors would add considerably and I hope more can be done this year.

In 1950 the Boston Medical Library will be seventy-five years old. It is planned to celebrate its birthday with a dinner at least, and perhaps some other activity. I hope also that a campaign may be started to raise the necessary $75,000 to complete our much-needed stacks.

I fear I may become tiresome about these stacks but unless they are installed the Library cannot serve its members efficiently. To climb stairs and mount scaffolding to locate volumes in temporary cases is exhausting and takes time. We must soon have the stacks and elevator.

We should continue our effort to increase our fellowships, for, as I have said before, the fellows are the legal corporation of the Library. They are the custodians of its treasures, and the responsibility should rest on many shoulders.

I wish again to express my great appreciation of the work already accomplished by the Librarian and the Director, and I am sure you would wish me to extend your thanks to them also. I want also to thank the Secretary and Treasurer and the members of the Board of Trustees for their whole-hearted co-operation. I think the Treasurer should have a little extra for his several efforts to obtain additional funds. If they come to naught it is certainly no fault of his.

I will leave to the Librarian the pleasant duty of informing you of our recent accessions and of the present state of our collections.

On the whole the prospect looks bright for continued prosperity and usefulness of this collection of books, one of the largest and most valuable medical libraries in the country.

WALTER G. PHIPPEN

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

RETROLENTAL FIBROPLASIA

The National Society for the Prevention of Blindness has circularized directors of maternal and child health with the following material, asking them to bring it to the attention of physicians.

"Retrolental fibroplasia, the presence of an opaque membrane behind the lens, was described by T. L. Terry, of Boston, in 1942 as a cause of blindness among premature infants. In a recent study covering various American cities, the incidence of the disease in 1301 premature infants weighing less than 1810 gm. (4 lb.) at birth was 7.6 per cent. It is recommended, therefore, that infants who were below this weight at birth be given a careful ophthalmoscopic examination at the age of six to nine months. Earlier than this the opaque membrane may not be seen except at the extreme periphery of the retina. Ophthalmologists interested in observing the development of the condition may want to see the infants in the early stages to look for dilatation, tortuosity and thickening of the retinal vessels, exudate and evidence of separation of the retina.

"The etiology of retrolental fibroplasia is unknown. Almost all reported cases have occurred in premature infants. Many theories of the causation have been discussed, some relating to the mother's condition during pregnancy, and others relating to nutrition, drug therapy and health of the infant. It is not now believed to be produced by the lights present in incubators.

"Treatment at present is not satisfactory. Some of these babies develop glaucoma and other eye conditions, so that they should be under ophthalmologic supervision."

BIBLIOGRAPHY

Krause, A. C. Congenital encephalo-ophthalmic dysplasia. *Arch. Ophth.* **36**:387-444, 1946.
Owens, W. C., and Owens, E. U. Retrolental fibroplasia in premature infants. *Tr. Am. Acad. Ophth. & Otol.* 18-41, September-October, 1948.
Reese, A. B. Retrolental fibroplasia. *Am. J. Ophth.* **31**:623-625, 1948.
Terry, T. L. Extreme prematurity and fibroblastic overgrowth of persistent vascular sheath behind each crystalline lens: preliminary report. *Am. J. Ophth.* **25**:203, 1942.
Terry, T. L. Retrolental fibroplasia. *Adv. in Pediat.* **3**:55-67, 1948.

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS

The April schedule for Consultation Clinics for Crippled Children in Massachusetts under the provisions of the Social Security Act follows:

CLINIC	DATE	CLINIC CONSULTANT
Lowell	April 1	Albert H. Brewster
Salem	April 4	Paul W. Hugenberger
Haverhill	April 6	William T. Green
Greenfield	April 11	Charles L. Sturdevant
Gardner	April 12	Carter R. Rowe
Brockton	April 14	George W. Van Gorder
Worcester	April 15	John W. O'Meara
Pittsfield	April 20	Frank A. Slowick
Fall River	April 25	David S. Grice
Springfield	April 26	Garry deN. Hough, Jr.
Hyannis	April 28	Paul L. Norton

Physicians referring new patients to clinics should get in touch with the district health officer to make appointments. Patients are seen by appointment only.

CORRESPONDENCE

DEPRIVATION AND RESTORATION OF LICENSES

To the Editor: At the meeting of the Board of Registration in Medicine held February 17, it was voted to revoke the registrations of Dr. Benedict Kudish, 526 Harvard Street, Brookline, and Dr. Allister F. MacDougall, formerly of Westford, and to restore the registration of Dr. Abraham Freitag.

GEORGE L. SCHADT, M.D., *Secretary*
Board of Registration in Medicine

State House
Boston

NOTICES

ANNOUNCEMENTS

Dr. Allen G. Brailey announces the removal of his office from 1101 to 1180 Beacon Street, Brookline.

Dr. Robert W. Wallace, of Westwood, has assumed the home and practice of Dr. George A. Small, 81 Walpole Street, Norwood, who has retired from general practice to prepare for the American Board of Anesthesiology.

EDWARD K. DUNHAM LECTURES

The Faculty of Medicine of Harvard University has announced that the following lectures on the general topic "The Cerebral Cortex of Man" will be delivered by Dr. Wilder Graves Penfield, professor of neurology and neurosurgery, McGill University Faculty of Medicine, and director, Montreal Neurological Institute, under the Edward K. Dunham Lectureship for the Promotion of the Medical Sciences:

Monday, March 28. Localization of Function.

Wednesday, March 30. Ictus Epilepticus (Physiological Observations on the Mechanism of Cerebral Seizures).

Friday, April 1. The Anatomy of Hallucinations, Dreams and Memory.

These lectures will be held in the amphitheater of Building D, Harvard Medical School, at 5 p.m., on the days indicated.

GREATER BOSTON MEDICAL TECHNOLOGISTS

A meeting of the Greater Boston Medical Technologists Association will be held in the operating-room amphitheater of the Children's Hospital, 300 Longwood Avenue, Boston, on March 29 at 8 p.m. Dr. William Freeman will speak on the subject "The Massachusetts Red Cross Blood Program and How It Affects You."

There will be an announcement about the state conference in April.

94TH INFANTRY DIVISION LECTURE

The 94th (Bay State) Infantry Division is sponsoring a series of monthly lectures by prominent physicians in their respective specialties. The second lecture will be held at the Reception Building, Boston State Hospital, Morton and Harvard Streets, Dorchester Center, on Wednesday, March 30, at 8 p.m.

Dr. Walter E. Barton will speak on the subject "Psychiatric Treatment in Hospitals."

All interested physicians, whether reserve officers or not, are cordially invited to attend this carefully planned program. Reserve officers will be given one point credit. Excellent films will also be shown during this period.

BOSTON GASTROENTEROLOGICAL SOCIETY

A meeting of the Boston Gastroenterological Society will be held at 12 noon in the Auditorium of the United States Marine Hospital, 77 Warren Street, Brighton, on Wednesday, April 6. The medical and surgical staffs of the hospital will present unusual medical and surgical gastroenterologic cases.

TUFTS MEDICAL ALUMNI ASSOCIATION ANNUAL DINNER MEETING

The Tufts Medical Alumni Association will hold its annual dinner meeting at the Hotel Somerset, Boston, on Wednesday, April 6, 1949, at 6:30 p.m.

The guest speaker is Dr. Leonard A. Scheele, surgeon-general of the United States Public Health Service.

Other speakers include Dr. Leonard Carmichael, president of Tufts College; and Dr. J. L. Lochner, Jr., secretary, New York State Board of Registration in Medicine. Dr. Roy J. Heffernan will preside.

The twenty-five-year class will hold its reunion also on this date.

AMERICAN SOCIETY OF ANESTHESIOLOGISTS

A joint meeting of the American Society of Anesthesiologists and the Southeastern Section of the Society will be held at the Statler Hotel, Washington, D. C., from April 7 to 9. There will be no registration fee for the meeting.

The program will include lectures, operative clinics at Georgetown and George Washington University hospitals, scientific exhibits, a cocktail party and a banquet.

NEW ENGLAND SOCIETY OF ANESTHESIOLOGISTS

A meeting of the New England Society of Anesthesiologists will be held in the auditorium of Building A, Boston University School of Medicine, 80 East Concord Street, Boston, on Tuesday, April 12, at 8 p.m. The scientific program will consist of the following:

Pharmacological Factors Influencing Collateral Respiration: Possible relation to the etiology of pulmonary complications. Ralph D. Alley, M.D., of the Department of Surgery, Yale University School of Medicine.

Pulmonary Ventilatory and Respiratory Function Determination Methods. Donald Rayl, M.D., resident in surgery, Uncas-on-Thames (Norwich State Tuberculosis Sanatorium), Norwich, Connecticut.

Artificial Respiration by Electrical Stimulation of the Phrenic Nerves. Demonstration by Stanley Sarnoff, M.D., of the Harvard Medical School Department of Applied Physiology.

Physicians and medical students are invited.

AMERICAN COLLEGE OF CHEST PHYSICIANS

The Board of Examiners of the American College of Chest Physicians announces that the next oral and written examinations for fellowship will be held in Atlantic City on June 2, 1949. Candidates for fellowship in the College who would like to take the examinations should communicate with the executive secretary, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois.

The fifteenth annual meeting of the College will be held at the Ambassador Hotel, Atlantic City, from June 2 to 5. An interesting scientific program has been arranged for this meeting, and speakers from several countries are scheduled to appear.

AMERICAN ASSOCIATION OF RAILWAY SURGEONS

The sixty-first annual meeting of the American Association of Railway Surgeons will be held at the Drake Hotel, Chicago, on Thursday, June 30, Friday, July 1, and Saturday morning, July 2.

An exceptionally interesting and instructive scientific program will be given from 10:00 to 12:30 on each of the three mornings, and from 2:00 to 4:30 on the first two afternoons.

The morning sessions will include twelve papers on various medical and surgical subjects, presented by outstanding authorities. The two afternoon sessions will be devoted to symposiums on "Lesions of the Bones and Joints" and "Intrathoracic Disorders."

The annual dinner will be held at the Drake Hotel on Friday evening, July 1.

Room reservations may be made at the Drake Hotel or at the nearby Knickerbocker Hotel.

There will be a technical exhibit in conjunction with the scientific meetings.

(*Notices concluded on page xiii*)